REPORT

ON

THE NATURE OF KALA-AZAR

BY

MAJOR RONALD ROSS,

INDIAN MEDICAL SERVICE.

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REPORT

ON THE

NATURE OF KALA-AZAR.

I.—PRELIMINARY.

Limits of the Present Enquiry.—My study of kala-azar was made under the following circumstances:—On the 17th February 1898 I was placed on special duty for six months under the Director General, Indian Medical Service, to investigate malaria and kala-azar. In this work I understood that my attention was to be devoted principally towards discovering the exact mode in which infection by malaria takes place. As regards kala-azar, I concluded that the study of that disease was admitted within the scope of my duties, chiefly because it had just been pronounced by Captain Rogers, I. M. S., to be a malarial disease, while it had long been accepted as a communicable one—a combination which, if Roger's conclusion be correct, promised to make the subject a very profitable one for enquiry in respect to the principal object of my deputation.

Before commencing actual work the question as to the best means of attacking the research entrusted to me was considered. It had long been obvious that the precise mode of infection by malaria could be ascertained only by the discovery of the life history of the parasites of malaria outside the human body. The subject was one with regard to which we knew nothing for certain at the time; but a little previously some indications had been obtained which went to show that these parasites can undergo development in mosquitoes. I decided then to begin my labours by following this clue as far as it would lead.

The difficulty generally felt with regard to Roger's opinion of kala-azar, that it is malarial fever, appeared to lie in the fact of the disease being communicable from the sick to the healthy, whereas in general acceptation malarial fever is not supposed to be transferable in this manner—in other words the subject of kala-azar was bound up in the more general problem which it was my chief duty to examine. Hence, on all grounds, I felt it better to postpone the consideration of kala-azar to that of the larger subject; and may add that I obtained the permission of the Director General to do so.

I proceeded, therefore, to attack this larger subject at once. The result has already been reported [1 and 2], but may be touched on here in view of its possible applicability to the present subject. Confining my attention to the malaria of birds, I ascertained by means of numerous experiments that proteosoma, Labbe, one of the so-called malaria parasites of birds, is capable of living and growing in a species of mosquito—a fact which established the truth of the indications just referred to regarding human malaria [1]. Further researches [2] showed that the mosquito stage of the avian organisms produces certain delicate thread-like reproductive elements which have the power of entering the veneno-salivary gland of the insect; suggesting that these bodies are meant to be injected, together with the secretion of this gland, into the wound made by the bite of the mosquito, thus causing infection in the insect's victim. Easy and complete proof of this theorem was next obtained by the experimental infection of healthy birds. Mosquitoes fed a week previously on birds containing the parasites of avian malaria were permitted to bite healthy birds. Nearly 80 per cent. of these contracted the disease in a few days under circumstances which leave no doubt as to the infection being due to the bites of the infected mosquitoes.

These researches occupied six months; during which, although I was able to examine cases of malarial fever and ankylostomiasis in the Darjeeling terai, it had been impossible to touch kala-azar. My special duty was now, however, extended for another six months, and I felt it time to take up my duties in this

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respect. Personally, I should have preferred to postpone the study of kala-azar until the general laws of infection by malaria were, if possible, ascertained by a completion of the study of proteosoma, which offers peculiar facilities for the purpose; but owing to the gravity of the epidemic in Assam, and to the fact that the nature of it was still being contested in the professional press, I thought that I might be expected to make some study of it at this point, even at the the cost of interrupting the logical course of the research. Accordingly, after spending a few weeks in the Darjeeling District on the examination of a disease called kala-dukh or kala-jwar, which is prevalent there, I went to Assam.

I arrived at Gauhati, Assam, on the 11th September, and proceeded at once to Nowgong, where, I had been told by the Sanitary Commissioner of the Province, numerous cases of kala-azar were to be found. I remained in the Nowgong District, chiefly in Nowgong itself, for six weeks; during which I took the statements of four medical officers of the district with regard to the disease; satisfied myself as to its identity; examined its pathology; and compared it with other sickness in the locality. At the end of that period, being of opinion that nothing was to be gained by a further study at that season of sufficient importance to delay any longer the pressing work on the general theory of malaria which remained to be done in the short time left to me, I requested permission to return to Calcutta. The permission was granted; and I was directed at the same time to submit my report on kala-azar as soon as possible.

It will be perceived that a complete study of the whole subject was scarcely possible in so brief a period. Fortunately the copious literature already in existence has previously dealt with many details, and I was able to concentrate attention on a few important questions, namely, those which had been left indeterminate at the time. In effect it will be seen the work has practically limited itself to a study of the *nature* of the disease; the epidemiology must be left untreated for the present as being an incident in a wider investigation.

2. Analysis of Existing Literature.—The literature on kala-azar, already voluminous, is to be found chiefly in the Annual Sanitary Reports of Assam from 1882 onward; in two special reports [3 and 4] written by Major Giles and Captain Rogers, both of the Indian Medical Service, as a result of a year's investigation made by each; in a controversy on the subject in the medical press [5, 6, 7, 8, 9, 10, 11, 12, 13]; and in Manson's Tropical Diseases [14].

In considering this literature briefly I propose first to refer to those points on which there is pretty general agreement.

The high *death-rate* of the disease is established by very numerous reports and statistics.

There is no doubt that it is an *epidemic* disease; this is certain from its progress up the Brahmaputra valley. Though it appears to have existed for many years in the Garo Hills, it was not officially noticed until 1882, when an investigation by Mr. McNaught, then Civil Surgeon of Tura in the Garo Hills, is recorded in the Sanitary Report. After this date the disease was observed to spread slowly up the valley, through the Goalpara, Kamrup, and Gauhati districts, abandoning each in turn, up to the Nowgong District, which it reached in 1889, and where it is now present. It has also spread to the Tezpur and Mangaldai districts. Further details of this progress will be found in Roger's Report [4]. The facts on this point, based as they are on numerous official reports and on the experiences of many district officers, medical and civil, are, I think, incontestable.

While the capacity of kala-azar for spreading from point to point has never been called in question, the opinion seems to have prevailed at first that its extension is due, not to direct communicability from the sick to the healthy, but rather to the progression of certain climatic (?) conditions favourable to its existence; see for example Dobson's opinion that it is not contagious, quoted by Rogers [4, p. 4]; see also [4, p. 5]. Later, however, when it was seen how frequently isolated villages, or the inmates of one house, or members of one family living in different houses, became infected, while neighbouring villages, houses and families escaped, it became impossible to deny the *communicability* of the disease. The fact is accepted both by Giles [3, p. 27] and by Rogers [4, p. 164]; also by the medical officers, whose statements are

given in the appendices; also in most of the literature; and most certainly by the people themselves, who have the best opportunities for judging. Giles deals very effectively with this point in Section IV of his report; and Rogers in Section VII of his.

I am of opinion, therefore, that the following facts about kala-azar may safely be accepted: it is very deadly; it constitutes an epidemic; it is communicable from the sick to the healthy in some unknown manner.

On two other important points, however, namely, the nature of the disease and even its very symptoms, there has been a notable difference of opinion.

At first it seems to have been assumed that kala-azar is malarial; when, however, the fact of its communicability just referred to became more and more apparent, doubt began to be expressed on this head, and Dr. Giles was directed to investigate the matter. He came to the conclusion that the disease is ankylostomiasis, or rather perhaps "a mixed anæmia brought about by ankylostomiasis acting on a population worn down by chronic malarial poisoning" [10], and explained the communicability of the disease very satisfactorily by his brilliant researches on the life history of the ankylostomum.

For a short period after the publication of Giles's report the medical profession in Assam appear to have accepted his views; by degrees however, to judge from the literature in the Annual Sanitary Reports, when the profession began to acquire greater familiarity with the disease, and when, especially, Dobson published his paper [15] on the wide prevalence of the ankylostomum among coolies imported into Assam, Giles's conclusions were objected to by many (read Roger's Report, Section I). Accordingly, another medical officer, Captain Rogers, was deputed to reopen the subject. He arrived at the conclusion that kala-azar is not ankylostomiasis, but malarial fever. His results were, however, questioned by Giles [7], Thornhill [9], and others [8, 14]. To these criticisms he replied at length [12].

It should be mentioned here that Captain Harold Brown has lately reported on a disease called kala-dukh, now prevalent in the Purnea District of Bengal [16]; and that I have independently become acquainted with a disease in the adjoining Darjeeling District, called indifferently kala-dukh or kala-jwar. These diseases will be described later (paragraphs 9 and 19).

3. The Main Questions at Issue.—To sum up, the literature of kala-azar leaves two questions still at issue, namely:—

(*a*) What is the nature of kala-azar?

(*b*) Supposing it to be malarial fever, as Rogers says it is, how explain its communicability?

It will be perceived that the first question must be satisfactorily disposed of before the second one need be attempted. Those who adhere to Rogers' opinion may complain that this has already been done by him in his able report; but in view of the fact that the profession did not appear absolutely to accept his conclusions, while some early observations of mine on the disease tended to throw doubt on them (paragraph 13), I felt it would be useful and even necessary to examine the matter again before attempting to consider the difficult subject of the communicability of the disease, which, as I have already said, it was my special province to examine.

On studying the recent discussion on this subject, we perceive that there is a divergence, not only in matters of opinion regarding the nature of the disease, but also in matters of fact regarding its very symptoms. According to Giles the disease is primarily an anæmia; with a general subnormal temperature, only occasionally, if at all, broken by slight attacks of fever; and "a very variable amount of splenic enlargement" [3, p. 11]. The enlargement of the spleen in some of the cases seen by him he attributes to the frequent existence of that symptom in malarious Assam. With regard to fever he remarks, "I have strong reason for believing that ankylostomiasis does often commence in a pyrexial attack" [p. 62]; otherwise, I gather, he attributes any fever which may be present to an accidental malarial infection. The subnormal temperature, he declares, "and the profound anæmia, were the most marked clinical characteristics of the disease with which I had to deal" [p. 11].

With Rogers, on the other hand, "fever is the most essential and constant feature of the disease," and "true cases of kala-azar invariably begin with fever [4, p. 38]. The spleen is always enlarged in some stage or other of cases

of kala-azar, but it is not so much the frequency of its occurrence as the constancy with which it attains to a very considerable size; that is the most remarkable feature of the disease" [p. 41]. "The liver was enlarged in 93 per cent. of the cases" [p. 41]. The anæmia, though present in 93 per cent. of the cases, is secondary to the fever [p. 45].

To be brief, with Giles kala-azar is an anæmia; with Rogers it is a fever.

With such differences as to facts it is scarcely surprising that there should be differences in the deductions drawn from them. It would be impossible, standing on Giles's basis, to admit the disease as malaria; equally impossible from Rogers' standpoint to accept its being ankylostomiasis.

It is evident, without further discussion, that there has been a considerable confusion of identity; and it is therefore necessary, before going further, to obtain a perfectly clear clinical picture of the disease.

II.—THE SYMPTOMATOLOGY OF KALA-AZAR.

4. The Identity of the Disease in the Nowgong District.—In one respect I was fortunate in having been directed to the Nowgong District. Kala-azar has existed there for eight years, and has caused such a large mortality that people are as familiar with it in the place as in other parts of India they are familiar with cholera.

I was equally fortunate in another respect. The Civil Surgeon of the district is Captain McNaught, who, as already mentioned, was the first to investigate the disease when attention was drawn to it in the Garo Hills in 1882. He has consequently been in a position to observe it for sixteen years; and has watched its procession from the Garo Hills, where it commenced, to Nowgong, where it now prevails, and where he daily sees numerous cases of it. If, then, Captain McNaught is not clear as to the identity of kala-azar, I do not know who is likely to be so.

Doctors Lavertine and Dodds Price, who practise in the neighbourhood of Nowgong, and Major Macnamara, I.M.S., Civil Surgeon of Tezpur, have all been familiar with kala-azar for years, and all expressed themselves to me as being quite confident regarding its identity.

I find that the statements regarding the disease which these gentlemen were so very kind as to give me, and which are reproduced verbatim in the appendix to this report, agree in the essential particulars with each other, and also with statements made to me by various medical subordinates who have long known the disease, and by many of the patients themselves.

On the whole, then, I feel it impossible to entertain any doubt as to the identity of the disease, at least as now existing in the Nowgong District.

5. The Clinical Picture of Kala-Azar in the Nowgong District.—In order to throw as clear a light as possible upon this important point, I think I cannot do better than give my own experiences in the order in which they were obtained.

I confess that the picture which had formed itself in my mind after reading the conflicting literature of the subject, was one which is well expressed by Manson [p. 191], and which I think has been obtained by most of those who have not actually seen the disease, in short, that of "a slow wasting disease, characterised by great and progressive debility."

My first impression of kala-azar was obtained at the large village of Roha, on the way to Nowgong, where there had been a severe mortality, although the epidemic was now on the wane. The first person whom I spoke to in the village was its Tahsildar, Sri Jut Gunahash Gasswami, a highly educated gentleman, who spoke English very perfectly, and himself had suffered from the disease. I pressed him to give me an account of his sickness; which he did in a manner which left no doubt as to the details. His evidence appears to me to be of value, since he has no medical theories to support; it is given in Appendix A in the words in which it was written down by me from his dictation some days later.

In his case there was no doubt about the identity of the disease, since at the time he was ill eight out of nineteen members of his family, and ten out of twenty-one servants, were attacked by it, eleven of them dying. He describes his illness as beginning with severe shivering followed by severe fever,

commencing suddenly and succeeded by similar attacks. Enlargement of the spleen and liver set in later, followed by swelling of the legs. The patient nearly died, but finally recovered on being taken to Benares, where he bathed in the Ganges. He was stout and perfectly recovered and well when I saw him.

In this case, then, the facts scarcely accorded with my forecast. We next entered the village, where the hospital assistant of the village dispensary had collected for my inspection a number of cases. I was told that there could be no possible mistake about the identity of the disease from which they suffered; it was only too well known in the village; and most of the patients shown to me had lost relatives from it. The appearance of all of them differed in one very important particular from what I had expected.

It was true that all were more or less emaciated, more or less anæmic; but what struck me at once in most of them was a characteristic protrusion of the abdomen caused by enlargement of the spleen and liver. Both these organs were greatly enlarged in all the cases. In some they were tender on pressure. The spleen often extended across to the right side of the abdomen, and the lower edge of the liver was felt three inches or even more below the lower end of the sternum. The majority of the cases had fever at the time (2 P. M. on the 13th September), as shown by the burning skin, pulsation of the carotids and dyspnœa. A second class of the cases, evidently more advanced, in which there was little or no fever, although the spleen and liver were still enlarged, exhibited a certain amount of anasarca, especially ascites, as witnessed by the very protuberant belly, and a slight dropsy of the feet. Only two of them suffered from dropsy of the face. While in some instances, especially in these two, there was certainly extreme anæmia, this symptom as well as emaciation were not generally so marked as I had anticipated, being in fact little apparent in not a few of the patients. On asking their history of some of them (several were children and lads, too young to attempt to deceive one [3, p. 10]) the invariable reply was that the sickness commenced with high fever followed by enlargement of the spleen and weakness.

It was impossible to accept for a moment the view that the fever and the enlargement of the organs were merely fortuitous complications due to the general prevalence of these symptoms among a malaria-stricken population. Had this been so the members of the crowd which stood round us would have been affected in a precisely similar manner and to precisely the same degree. This was not the case. Any general prevalence of these symptoms to the degree they existed in the patients before me would clearly have almost exterminated the whole population of Assam in a year or so. It was obvious that so extreme a tumefaction of the organs could in many of the cases end only in death. On the other hand, the surrounding crowd had every appearance of being free from these affections, at least to anything like the same extent. Kala-azar, as existing at Roha then, was evidently not a mere anæmia but a fever (and, I judged, a severe one) producing tumefaction of the spleen and liver, and a final cachexia.

Next day Captain McNaught showed me a number of cases of kala-azar in the Civil Hospital at Nowgong. He informed me that they were exactly like those which he had first seen in the Garo Hills. All of them, without exception, were cases of great tumefaction of the liver and spleen. In most of them there was constant fever; in some, œdema, especially of the feet and abdomen; while various degrees of anæmia and emaciation were generally present. They were obviously identical in nature with the cases which had been pointed out to me as kala-azar in Roha; and in nearly all of them there was the familiar history of relatives having suffered and died from the same disease.

I spent more than five weeks at Nowgong examining these and other cases; and before leaving took a statement from Captain McNaught regarding his experiences of the disease. Next I proceeded to the tea estates in the neighbourhood, where I conferred with Drs. Dodds Price and Lavertine, took their statements and saw some cases which they showed me. These were exactly like those which I had seen at Roha and Nowgong. Lastly, I met Major Macnamara at Tezpur, and through his courtesy was enabled to add his evidence to my collection.

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At this point a perusal of these statements (Appendix A) may be suggested. It will be seen that all these gentlemen are describing either the same disease, or else diseases indistinguishable from each other by their symptoms.

My own observations with regard to the clinical features are in general accordance with theirs.

It is obvious, then, that the disease now existing in the Nowgong and Tezpur districts and called kala-azar there is a very definite entity, characterised chiefly by fever, enlargement of the spleen, and in many cases by enlargement of the liver.

6. Symptomatology of Kala-Azar in the Nowgong District.—This being the case, I think that I may now safely proceed to discuss in greater detail the history and symptoms of the disease referred to. As the course of the sickness may last for years, it is impossible for me to describe the entire history altogether from my own experience; I can do so only from my own observations made on different cases taken at various points in their history and afterwards collated; from the more protracted observations of others; and from enquiries of the patients themselves. As I wish to give here the results only of my own enquiries and observations, I exclude previous literature on the subject.

The history and symptoms of cases of kala-azar as now existing in the Nowgong District are as follows:—

It is difficult to obtain any definite information regarding the prodromata. In cases 35 and 66 (paragraph 17) preliminary "uneasiness" and "feeling ill" are recorded. It must, however, be clearly understood that there is no gradual access by way of initial anæmia, emaciation, weakness, or dyspepsia; the dissolution of health is abrupt.

The onset is always characterised by fever [all]; often severe, sometimes very severe [McNaught]; severe [Macnamara]; generally severe [Lavertine, Price, Ross].

The fever may be continued [McNaught]; or remittent [all]; or intermittent [Lavertine, Price, Macnamara, Ross]; usually remittent [Macnamara]; not intermittent [McNaught].

It begins sometimes with rigors, sometimes with mere chilliness [McNaught, Ross]; rigors and chills are rare [Lavertine, Price, Macnamara]; chills occur especially in the intermittent forms [Lavertine, Price].

The fever lasts for 10, 14 or even 20 days [McNaught]; about a week [Macnamara]; from three weeks to three months [Lavertine and Price].

During this period the spleen and liver become slightly enlarged and often painful, sometimes even in a condition of inflammation [McNaught]; the enlargement begins generally after three or four weeks [Lavertine and Price]; generally after three months [Macnamara]. Some confusion has probably existed in these accounts in regard to the degree of enlargement referred to.

After the first febrile period there is generally an apyrexial period [all] which lasts for a week or two or more; indefinitely [McNaught]. This is followed by a second or third attack, or more attacks, of a similar nature to the first [all]; not preceded by rigors [McNaught]; but with apyrexial periods between [McNaught].

During the whole of this stage the spleen continues to enlarge in every case [all]. The liver also, in every case [all]; only in one-third of the cases [Macnamara].

Anæmia progresses with the illness [all]. There is an access of anæmia with each attack of fever, with improvement in the interval [Lavertine, Price, McNaught, Ross]; anæmia begins at the third or fourth month and is a continuously progressive anæmia [Macnamara]. It ultimately becomes extremely marked [Macnamara and Lavertine]; not so extremely marked [Price, McNaught, Ross].

Emaciation is progressive throughout [all].

By this time the tumefaction of the spleen has reached large proportions [all]. The liver also is enlarged, generally much so, in all cases [all except Macnamara]; typically so [Price, Ross]; only in one-third of the cases [Macnamara]. The organs are both tender and painful [McNaught, Ross]; there is no pain nor tenderness, but discomfort [Macnamara].

At this stage, too, "when the enlargement of the organs has reached a certain degree," "the temperature as a rule remains above normal day and

night" [Lavertine, Price, Ross]. "A low form of fever, which remains for weeks or even months," sets in [McNaught, Ross]. After the *first* attack of fever there are "slight attacks of fever which become more and more frequent, until eventually the temperature never falls to normal, lying between 99° and 101°F., though the patient is generally unconscious of it" [Macnamara].

This condition remains for months [McNaught, Ross]. There may sometimes be, however, intercurrent attacks of high fever [McNaught, Price, Ross].

Ascites and œdema of the feet, more rarely of the face, may be present [all].

There is often undoubted darkening of the skin [McNaught, Lavertine, Price, Macnamara].

Epistaxis frequently occurs [McNaught, Ross]; Macnamara has not noted it.

A stage of cachexia now sets in, during which the low fever disappears, while the spleen and liver decrease in size; the emaciation and darkening of the skin, however, remain, accompanied by extreme weakness [McNaught, Ross]. Lavertine and Price, while admitting the existence of this stage, do not note decrease of the organs. Lavertine observes now a subnormal temperature. Macnamara is doubtful on the point.

Diarrhœa and dysentery are common intercurrent affections. Pneumonia also occurs [McNaught, Price]; does not occur [Macnamara, Lavertine].

Death may happen at any stage [all, except Macnamara]; at the beginning from high fever; later from diarrhœa, pneumonia or asthenia, or [Lavertine] cancrum oris. It is more frequent in the later stages.

Quinine has little or no effect [McNaught, Lavertine, Macnamara]. Price says, however, "I think that quinine does do good; it is difficult to say, because when a case is cured we have our doubts whether it has been kala-azar."

The disease is communicable from the sick to the healthy [all]; only indirectly so [Price].

Further interesting details will be found in the Statements.

Owing to the acknowledged difficulty of distinguishing the early symptoms of the disease from those of malarial fever, they must be generally ascertained from enquiries of patients—a method which scarcely yields exact results, though, as has been shown, a general history of severe fever is always given. Such enquiries, while individually they are frequently unreliable, constitute in the aggregate a mass of evidence which it is impossible any longer to resist. I have depended for the facts not only on the four medical officers referred to, but many others—notably on the Reverend Mr. Moore, of the American Mission in Nowgong, who has seen very many cases in that establishment. In my experience, however, the evidence be sifted, it always returns to the facts just given.

We may now proceed to a more formal symptomatology based more upon my own conclusions.

I adhere to the division of the history into three periods, implied in the statements of Dr. Lavertine and Captain McNaught.

The *first stage* is that of recurrent accessions of acute fever separated by periods of apyrexia. It has not been possible to determine exactly the type of fever, nor to what extent it is preceded by rigors, nor whether the apyrexia is complete or not. To judge, however, from the evidence of Sri Jut Gunahash Gasswami, which is much more reliable than that commonly extracted from patients, usually peasants, the fever may be first remittent and afterwards intermittent, rigors being frequent. I have often obtained the same history from other patients, and am of opinion that rigors are more common than is supposed. Still I think that they may often be entirely absent. In many cases there is a history of an entire cessation of fever for intervals of weeks or months, followed by relapses; in others, again, a continuous low fever sets in almost immediately after the first attack of severe fever, and continues throughout, being, however, frequently interrupted by severe exacerbations. Macnamara's description of slight attacks succeeding the first fever, and becoming more and more frequent until a continued low fever is established, would suggest a progressive tendency towards something like Torti's subintrant fever; I think it more likely that in such cases the continued but low fever is really established early and exists throughout—see case 35, paragraph 17. It is useful to distinguish sharply between this persistent low fever and the frequent relapses or conflagrations of severe fever which McNaught and Price refer to.

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Enlargement of spleen and liver begins from the commencement of the illness. It is possible, however, that the tumefaction of the liver may be subsequent to that of the spleen. In my experience in Nowgong the liver was almost always enlarged.

Anæmia and emaciation set in early, being, I think, augmented after each attack of fever.

I am of opinion that œdema of the feet may appear even as early as the end of this stage.

About the darkening of the skin I cannot speak with any authority; but it would seem to appear early in some cases.

As the disease progresses the enlargement of the spleen and liver increases. The organs are tender on pressure as a rule, and a patient often complains of pain in them.

The *second stage* is that of established and still acute tumor of the spleen and liver, accompanied by a constant low fever; recrudescences of high fever may, however, still occur at longer and longer intervals, but I think are often entirely absent.

The splenic dulness generally occupies most of the left half of the abdomen, while the liver extends to two or three inches below the lower end of the sternum in the median line. The enlargement may often be less or greater than this in the case of both organs. There is generally tenderness of one or other, or of both—not acute, but sufficient to make the patient wince on pressure of them; while pain is frequently complained of, especially in the hepatic region. In most of the cases seen by me tumor of the liver was a marked feature. In some of the worst cases there was very evident thoracic breathing. A slight degree of icterus is often present.

The fever has two notable characteristics; the diurnal curve remains almost exactly the same day after day for weeks or even months, and the amplitude is not much—in other words, the type is extraordinarily constant, and the temperature has, comparatively to some other fevers, only a small range of variation. Several charts of this fever are given in connection with the cases in paragraph 17, and these characteristics will be noted in them. The history is not that of recurrent conflagrations of fever interrupted by intervals of apyrexia; it is that, so to speak, of a continuous chain composed of links always similar to each other. This fever will be discussed at length in Section IV; it is certainly the kind of pyrexia found by me in nearly all the cases in which exact thermometric observations were made under my own superintendence; and it is referred to by all the medical officers whose statements I have taken. I should add here that the diurnal exacerbations are not as a rule ushered in by rigors or even a feeling of chilliness, and that quinine appears to have no effect on the chart.

Anæmia is certainly pronounced at this stage, but in my experience it is not excessive. In nearly all the cases studied by me the tongue and conjunctivæ remained fairly red. So far as I could judge from mere qualitative examinations of the blood, the degree of anæmia remained constant at this stage.

Neither did I find the emaciation to be always extreme. A group of children suffering from pronounced kala-azar in the Civil Hospital at Nowgong were, most of them, quite fat, although their livers and spleens were enormously enlarged, and they suffered from the constant fever just described. This symptom would appear to depend largely upon the alimentation, and possibly on the degree of helminthiasis present.

Epistaxis is common at this stage.

A certain amount of ascites is almost always present in connection with the enlargement of the organs. The anasarca not unfrequently extends to the feet at this time; rarely to the face.

As the disease advances, if death has not occurred, the further enlargement of the organs ceases; they lose their tenderness; the fever gradually declines—ushering in the third stage.

The *third stage* is that of cachexia. The liver and spleen, still much enlarged, lose their tenderness, and may even, I think, return to their normal dimensions. The fever has disappeared, giving place perhaps to a continuously subnormal temperature. Ascites has generally increased, but, on the other hand, dropsy of the feet is, when present, less than before. The anæmia is not very

extreme. Emaciation depends on the degree of alimentation. Intercurrent affections—diarrhœa, dysentery, pneumonia—appear to be common; the diarrhœa, however, may be a part of the pathological process of the disease itself at this stage, and seems in many cases to be followed by a rapid reduction of the liver and spleen.

If death has not yet occurred from fever or an attack of some complicating disorder, it may now follow as the result, apparently, of pure asthenia. On the other hand, recovery may ensue, but only from the early part of this stage—the tumefaction of the organs, especially of the liver, is gradually resolved, the blood regains its corpuscular richness, the emaciation, fever and ascites disappear. When, however, cachexia is once firmly estalished, recovery appears (?) to be impossible.

To sum up—*the characteristics of the three stages are recurrent conflagrations of high fever with rapid enlargement of the liver and spleen in the first stage; great tumefaction of the organs with constant low fever in the second stage; and cachexia in the third stage.*

It is impossible to fix exactly the duration of each stage. I am disposed to put the first stage at one or two months only, and the beginning of the third stage at nine months or a year, or even more, from the commencement of the illness.

In the above description—which I must confess is far from a full one—I have purposely avoided reference to many secondary symptoms, such as cardiac, nervous, renal, or digestive ones. Any sufficient study of these requires a long observation of the disease; and a consideration of them is not essential to the main object of this report.

7. Diagnosis.—Are there any diseases in the Nowgong District with which kala-azar as just described may be confounded? There are two—paludism, and a species of anæmia generally complicated with dropsy. The differential diagnosis (if there be any difference) must be considered in full only after the pathogenesis of kala-azar has been examined. At present I will confine myself to a few remarks on the subject.

It will have been already noted that the symptoms of kala-azar as just given are, if not identical with, yet very closely similar to those of ordinary malarial fever (better called paludism). I have frequently observed that when I have shown a case of fever in its earlier stages to a medical officer or his subordinates in the Nowgong District, and have asked for a definite pronouncement as to whether the case was one of kala-azar or not, the statement could not be given. On showing more advanced cases, however, in which the liver and spleen were much enlarged, the answer was generally ready enough, and in the affirmative. It would appear then that kala-azar can only be diagnosed when it has reached the second stage.

Here again the same difficulty occurs, because a similar second stage of enlargement of the organs is met with also in chronic paludism. How make the distinction even here? It would appear from the statements that a history of the relatives of the patient having suffered from a like malady, the refractoriness of the disease to quinine, and perhaps, according to Price but not according to Macnamara, the great enlargement of the liver, are relied on for the diagnosis.

It will be confessed that these means of diagnosis are scarcely convincing. It would appear as if early cases of fever, which recover before tumefaction of the organs has occurred, are cases merely of ordinary fever, while those in which the tumefaction has taken place are cases of kala-azar. I noticed also that there were scarcely any recorded cases of "malarial cachexia" in the district, though from the number of cases of recent malarial infections more of these may have been expected to exist there. Are old cases returned as kala-azar?

These questions will be dealt with best when the actual relations between kala-azar and paludism are discussed.

With regard to the anæmia with dropsy just referred to, I may remark that I saw several cases of the disease in the Nowgong District, and that the medical men in the province are perfectly familiar with it. The symptoms are profound anæmia, and, generally towards the later stages, a considerable degree of dropsy, extending to the face; but there is no history of high fever

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and no enlargement of the spleen or liver — except occasionally, and to such a small degree as may be explicable on the ground of the general malarial taint in the population.

There is no question of mistaking this disease for kala-azar of the first or second stages; but I think it may be confounded with kala-azar of the third stage — especially in those cases in which the enlargement of the organs has diminished toward death or as a consequence of diarrhœa. The differential diagnosis will be referred to in paragraph 41; and I mention the disease here only as a leading to the following remarks.

8. The Identity of Kala-Azar Generally.—It frequently happens that when an epidemic first appears in a locality — as, for instance, in recent epidemics of plague or influenza — many kinds of cases are put down as instances of the dreaded pestilence. This must be especially the case when the actual epidemic disease has no very prominent symptoms — such, for example, as always serve for the identification of cholera or small-pox; and still more so when it is a protracted disease, extending over many months, during which it perhaps largely changes its characteristics and finally causes death only after a long ill-defined cachexia. It would indeed be unreasonable to expect at once complete and general identification of the disease in outbreaks of this nature; while in one place and at one time a correct notion of it would be formed, it is quite possible that in others any fatal and ill-known sickness which happens to be prevalent there at the same time will be mistaken as an instance of it; and it would not be until after a considerable period that the profession and the public would gain sufficient familiarity with the true epidemic disease to make no more errors in regard to its identity.

Such, I cannot help thinking, has been notably the case with kala-azar. It was peculiarly unfortunate that at the moment when the epidemic first appeared there should have been another disease prevalent in the same locality — a disease little studied in Assam at the period, and which, as has just been pointed out, may be confounded with the third stage of true kala-azar, namely, the "anæmia with dropsy."

Since then, however, the profession has had sixteen years' experience of kala-azar; it has been studied in many parts of Assam; and a thorough understanding has been arrived at as to the general difference between the two diseases. The result is that kala-azar is now recognised in the country to be a fever with enlargement of the spleen and liver, and not a mere anæmia.

In the clinical description of kala-azar which I have just given, I have been careful to express it as being applicable only to the kala-azar of the Nowgong District, to which my observations of the disease were confined; and I have expressly avoided in it all reference to descriptions already given in existing literature—partly for purposes of comparison, and partly because I wished to present only such evidence as I myself was able to collect. But if this literature be now consulted — especially the Annual Sanitary Reports, Rogers' Report and Section V of Giles's Report— it will, I think, be understood that my definition of kala-azar in the Nowgong District applies equally to kala-azar generally—that is, to the kala-azar which has been described by the large majority of medical men who have practised of late years in the affected tracts. The almost exact coincidence between my symptomatology and that of McNaught and Rogers, who have studied the disease, the one from its first appearance in the Garo Hills, and the other during a whole year's special investigation, will, I think, strike anyone who takes the trouble to compare our descriptions. Under these circumstances, then, I think, I may now venture to extend my definition to kala-azar generally, wherever it has existed in Assam.

It is, of course, still open to anyone to say that the disease here described is only a spurious kala-azar—that the true kala-azar is the anæmia with dropsy. Both diseases exist side by the side in the country; both cause a large mortality; both are communicable from the sick to the healthy; and I have no doubt that serious outbreaks of the anæmia, as of the fever, have occurred in isolated villages and tea-estates, and that the people themselves have frequently given the name kala-azar to cases really suffering only from the anæmia. Nevertheless, I think with Rogers that there is no doubt that the fever is the true kala-azar.

My reasons are that the prevalence of the anæmia is confined mostly to the tea-estates, and is not nearly so great on the whole as that of the fever, while it is the latter disease which has been described as kala-azar by nearly all observers from McNaught onward. Thus, in Nowgong, while there were very numerous instances of the fever alone, there were only two or three instances of the anæmia alone—which, moreover, had all come from tea-estates. Here, however, my own experience bears no authority compared with that of the medical men who have seen cases of both diseases for years, and who pronounce emphatically on the superior prevalence of the fever. When, further, we recognise from a perusal of the literature and of the statements appended to this report that it is the fever and not the anæmia which has almost always been described as kala-azar and is known as such at the present moment, we are inevitably driven to the conclusion that if there be two epidemics now co-existent in Assam, the epidemic of fever is far more formidable than that of anæmia, and is the one which has been and is generally recognised as kala-azar.

It is necessary, of course, to understand that the two diseases may often be concurrent in the same village and the same individual; but still it cannot be conceded for a moment that the term kala-azar is to be confined to a *combination* of them—that only such individuals as are suffering from the two together can be said to be suffering from kala-azar. While it is likely that the combination of the two diseases may be more formidable to a patient than each separately, at least in the first and third stages of the fever, it is not likely to enhance the illness to such an extent as to create practically a new disease with a very much greater mortality than each factor separately can produce. Those who have seen the fever and have noted the extreme gravity of the splenic and hepatic incidents, will find no hesitation in accepting its power of causing death without extraneous assistance. It is even possible to conjecture that the anæmia may be actually beneficial during the second stage of the fever; and, in fine, the "anæmia with dropsy" does not exist as a factor in many of the worst cases of the fever.

Those who are inclined to hold that kala-azar is a combination of the two diseases, the fever and the anæmia, have urged further that it is the latter which imparts the element of communicability to the product. This also is inadmissible. Each disease can be propagated only after its own kind — the anæmia can propagate only anæmia. Now, by an irresistible weight of testimony, it is known that a patient suffering from the fever called kala-azar propagates a similar *fever* amongst his relatives (compare, for example, the case of Sri Jut Gunahash Gasswami in the appendix), and that one after another these relatives are attacked, and suddenly attacked, by *all* the symptoms of the original case. If the anæmia were the only transmissible factor of the disease, such a patient would transmit only anæmia to his relatives, although he himself had suffered also from fever.

To put the matter in a perfectly clear light:—

The fever and the anæmia are quite distinct diseases, and both are communicable from the sick to the healthy.

If either were swept out of the country to-morrow the other would remain.

If the anæmia were to be swept away the mortality in the localities now suffering from kala-azar would be but little diminished.

If, on the other hand, the fever were to be removed, the present epidemic of kala-azar would cease and the mortality would return to its usual limits.

Some further remarks on the relations between the two diseases—a subject of the highest importance in tropical medicine generally—will be found in paragraph 41.

In conclusion, then, and after a quite impartial survey of the matter, I must record my adherence to the opinion already promulgated by Rogers—that true kala-azar is the fever with enlargement of the spleen and liver, and not the anæmia with dropsy.

9. Kala-Dukh and Kala-Jwar.—I have referred in paragraph 2 to a disease called kala-dukh now prevalent in the Purnea District of Bengal and lately investigated by Captain E. Harold Brown, M.D., I.M.S., [16]; and also to a disease seen by me in the adjoining Darjeeling District, called indifferently kala-dukh or kala-jwar. I now propose to give a brief description of these diseases.

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Regarding kala-dukh in the Purnea District Captain Harold Brown remarks:—"The people in these parts regard the disease as infectious, and in consequence, on the occurrence of a case in a village, the inhabitants of the uninfected huts leave the place and build themselves fresh habitations close by, generally within a quarter of a mile; the relatives of the infected people remain, however, unless a case terminates fatally, when every hut is deserted, and there is evidence of this having occurred in several of the villages which I visited."

Regarding the symptoms of the disease, he says:—"The history given by the great majority of the patients is that, at the outset, kala-dukh begins with fever, usually of an intermittent type; this being untreated is apt to recur at shorter intervals, a tertian becoming quotidian, and the fever eventually passing into a distinctly remittent or continuous type. A few cases die at this stage, as would be expected; but, as the characteristic symptom of the disease—pigmentation of the skin—has not had time to declare itself, these deaths are attributed to ordinary malarial fever. In the majority of cases, however, the fever lessens after having been remittent or continuous for four or five weeks, and a period of apyrexia follows, very variable in duration, sometimes lasting weeks or months, at others only a few days. At this stage the patient is weak and more or less prostrated; enlargement of the spleen has occurred, attended with a certain amount of anæmia; the patient is easily tired, is unable to work, and his digestion is impaired; but, unfortunately, the disease still remains untreated; the surroundings continue unaltered; the anæmia and the causes producing it are not combated, and the patient who, under more favourable circumstances, might soon improve under suitable treatment and diet, is left exposed to the original poison, the presence of which in his system is evidenced by the occurrence of irregular exacerbations of fever, each of which tends to aggravate the anæmia and splenic enlargement.

"If the intervals between the attacks of fever are long, the patient does not lose ground fast; but when, as often happens, there is fever of an irregular type every day, generally in the evening, the patient rapidly grows worse. The anæmia increases; œdema of the feet and face, with ascites, sets in; and the patient, too weak to walk, too ill to digest the ordinary food of the country, succumbs eventually either to diarrhœa or exhaustion.

"In the meantime darkening of the skin has occurred, most marked on the face and legs. In some cases this has affected the entire integument so equally that none but those who knew the patient before his illness could detect the fact, and I repeatedly had to accept the statement made by the patients or friends, strengthened as it was by comparison with a healthy individual who was produced for contrast, the patient and he having originally been of the same colour, generally a light copper."

Captain Harold Brown makes no mention of enlargement of liver; but for this it will be seen that his description accords very closely with that given above of kala-azar. It will be observed that he talks of the attacks of fever becoming subintrant in the early stage, and mentions that when the disease is established there is "fever of an irregular type every day, generally in the evening"—corresponding possibly with the "constant low fever" found by me in the second stage of kala-azar His interesting pathological work on the disease will be discussed later (paragraph 31).

My experience of kala-jwar in the Darjeeling terai was as follows. In May last, while working at malaria in the terai, I was informed by Mr. Dessa, Inspector of Police in the neighbourhood, that the natives there spoke of a very fatal disease which they call either kala-dukh or kala-jwar. They averred that it was communicable to such an extent that when one case entered a house the rest of the occupants were nearly sure to acquire it. Mr. Dessa added that he personally knew of several houses in remote villages where almost all the occupants had been taken ill and had died; and offered to show me cases.

This was before I had heard a word of kala-dukh in the Purnea District.

It was, however, not until late in August that I was able to study the disease. I then went with Mr. Dessa to the large village of Naxalbari, situated some ten miles away from the foot of the Himalayas, in the plain, where he informed me cases were procurable. Whilst there I examined thirty-four cases of local sickness, of which fourteen were said to be instances of kala-jwar,

while eighteen seemed to be ordinary paludism and two were probably "the anæmia with dropsy."

I may say at once that the appearance of the kala-jwar cases was in every respect similar to that of the more advanced cases of paludism; in fact it was impossible to determine how the people themselves drew a distinction. Moreover the general picture presented was almost identical with that of kala-azar, except that the liver was certainly not so frequently or so much enlarged. It rarely extended to two inches below the lower end of the sternum, and as a rule could be said to be only slightly enlarged; in one or two cases, however, it was as large as in kala-azar. The spleen was often enormous, in one case apparently filling the whole abdomen, and generally occupying half the surface. Neither the anæmia nor the emaciation struck me as being very severe; indeed some of the cases were almost fat and others showed a very fair blood.

Most of these patients were examined only once, and before noon. The temperature of all, except one, was above the normal, lying between 98·4° F. and 101° F., and averaging about 100° F. The exception had a temperature of 97·1° F. This raised morning temperature without any tendency to rigor suggests the "constant low fever" of paragraph 6; in fact almost all the cases were obviously in a condition corresponding with the second stage of kala-azar. I cannot speak definitely about any darkening of the skin, or of the exact history of the cases; but all agreed in saying that their illness commenced with high fever. Many of the patients, moreover, told me that relatives had suffered from the same complaint.

It would appear, then, from the similarity of the symptoms and the evidence as regards communicability of the diseases, that kala-dukh in the Purnea District, kala-jwar in the Darjeeling District, and kala-azar in Assam are all the same disease.

The result of my examination of the blood of the Naxalbari cases is given in paragraph 19.

10. Nomenclature.—Major Waddell, LL.D., I.M.S., furnishes me with the following details. *Kala* (Sanscritic) means *black* or *deadly*. *Dukh* (Sanscritic) means *suffering* or *pain;* literally disease, *i.e.*, want of ease. *Jwar* (Sanscritic) means *fever*, *i.e.*, raised bodily temperature. *Azar* (? Assamese) means *sickness;* but in Nowgong the words *jwar*, or *bimari* (Urdu), *illness*, are more frequently used by the people.

The popular use of the adjective *kala* does not appear to me to imply necessarily blackening of the skin. Perhaps the original meaning was *deadly*. It is possible that the meaning has now become transferred to the more literal significance of the adjective *black*. Thus *black death* meant only plague originally; until, the word stimulating the imagination, people saw a blackening effect in the disease which it does not possess. Just, possibly, the same thing has happened in kala-azar.

III.—PATHOLOGICAL ENQUIRY.

11. *Prima Facie* Evidence regarding the Nature of Kala-Azar.—A clear clinical picture of kala-azar having been arrived at, it is now possible to examine more deeply into the nature of the disease. We can already draw some important inferences regarding this from the description of its grosser features just given.

Throughout the tropics generally there is a group of animal parasites of man prevalent almost everywhere, but more so in some localities than in others. These are, several species of worms—filariæ, round-worms, whip-worms, ankylostomes, and certain flukes; some minute protozoal parasites of the liver and intestine, notably amœba coli and cercomonas or trichomonas intestinalis (the protomyxomyces coprinarius of Cunningham); and at least three species of protozoal parasites of the red corpuscle.

I have found most of these very frequently in various parts of India—the Southern Presidency, Rajputana, Bengal, Assam; namely, filariæ nocturnæ, round-worms, whip-worms, ankylostomes, amœbæ coli and cercomonads, and the parasites of the red corpuscle. They have also been noted here and there by many observers; and it is likely that they all have a very wide prevalence throughout the Indian Empire. See for instance [15, 17, 18, 19, 20, etc.]

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They were all frequently observed by me in Assam. In Gauhati, in the excreta of 5 hospital patients examined, I observed the eggs of round-worms in 2, of whip worms in none, of ankylostomes in 4, amœbæ in 3, and cercomonads in 1. In Nowgong, in the excreta of 17 patients examined, round-worms were present in 8, whip-worms in 11, ankylostomes in 11; amœbæ and cercomonads were not carefully searched for. In addition to these amphistomum hominis occurred in two out of eight autopsies. These results agree with those of other observers (except in regard to the protozoal parasites, which have been much overlooked in India); and there is no doubt that the entozoa referred to are very common in Assam. The parasites of the red corpuscle were found by me in 30 out of 73 people searched for them, mostly cases of fever, in Nowgong.

In considering the question whether any of these parasites cause any particular disease, it is necessary to show not only that the parasite is present at one time or another in the course of the disease, but also that it can and does produce the symptoms—the disease must be looked at as a whole and we must ask ourselves whether, judging from our previous knowledge of the parasite, the symptoms are likely to the produced by it.

We may, for example, rest assured that none of these organisms can cause small-pox, or cancer, or influenza. On the other hand, it is often *primâ facie* possible that a case of anæmia may be due to ankylostomes, and of fever to the parasites of the red corpuscle.

Applying this test to the two diseases described and differentiated in paragraphs 6, 7, 8, and 9, it will be obvious at once that the "anæmia with dropsy" may be due to ankylostomes and the "fever with enlargement of the spleen and liver," to the parasites of the corpuscles. At the same time it will be equally apparent that the fever in question cannot be produced by the ankylostomes, nor the anæmia (without fever) by the blood parasites.

As a matter of fact, with regard to the anæmia, it is already established by the labours of Ruddock, Giles, Campbell, and others (in Assam alone) that it is produced, at least in the majority of cases, by the ankylostomum duodenale —that the anæmia with dropsy which I have so frequently referred to is, in fact, ankylostomiasis.

Similarly, we may rest equally assured that the fever with enlargement of the spleen and liver, called kala-azar, is *not* ankylostomiasis. So evident is this fact that I think we may safely accept the opinion of Sir W. R. Kinsey [11], himself a great authority on ankylostomiasis, to the effect that no elaborate discussion of the matter is required. The symptoms of ankylostomiasis, pure and simple, frequently studied in Europe, Egypt, Ceylon, America and elsewhere, are quite different and remote from those of kala-azar pure and simple. If kala-azar has ever been thought to be ankylostomiasis the error has been probably due, as I have suggested in paragraph 8, to a confusion as to the identity of the disease at the beginning of the epidemic. If kala-azar be defined as an acute fever, especially a fever with enlargement of the spleen and liver, it cannot be ankylostomiasis. The deduction springs at once from the definition.

Rogers, not contenting himself with a simple discrimination of this nature (which, I confess, appears sufficient to me), has gone further and has argued the matter at great length. In [12, p. 249] he gives an excellent summary of the differences between kala-azar and ankylostomiasis; while in his report [4] he examines some of the differences between the anæmia of the one and of the other disease. It is perhaps to be wished that he had increased our indebtedness to him by actually giving the blood-counts in sufficiently long series of cases accompanied by counts of the ova of the worms found in the excreta. The short time at my disposal rendered it inadvisable for me to attempt any confirmation of his work in this respect; but I think that, all things considered, it is impossible to avoid at any rate the conclusion arrived at by him.

The fact is that ankylostomes can no more be the cause of kala-azar than the other worms just referred to can. The effect of all of them on the economy is perfectly well defined. We know that in sufficient numbers some or all of them may produce such symptoms as emaciation, dyspepsia, diarrhœa, even slight fever, anæmia, eclampsia, icterus, ulceration of the bowel, and so on. Lately, moreover, observations have been recorded tending to show that worms secrete a toxic material which may influence the system in many ways. Manson in the discussion on kala-azar before the Royal Medical and Chirurgical

Society [11, p. 280] forcibly suggested this. Nevertheless it is quite obvious that, whatever effects these worms can and do produce, they cannot and do not produce the high fever with sudden onset and the great enlargement of the liver and spleen which are the characteristics of kala-azar. Even if a theory of intoxication may lead us to suppose hypothetically that they may do so, we know, as a fact, that they do not. These worms exist in Europe and in many places and individuals where anything like the symptoms of kala-azar are quite unknown. In short, all of them must be exonerated from being the pathogenetic agents of the disease.

I propose then to exclude further discussion of the question from this report. How far ankylostomes complicate individual cases of kala-azar will be examined in paragraph 41.

12. Survey of the Question.—To judge from the symptoms already given, what strikes us as being possibly the nature of kala-azar?

The reply must be that of all known diseases kala-azar, as described in paragraph 6, has the closest resemblance to the disease produced by the protozoal parasites of the red corpuscle, that is, to malarial disease. The sudden accession of high fever, of remittent or intermittent type, the frequent recurrence of similar attacks, the gradual tumefaction of the spleen and liver, even the occurrence of epistaxis and the final cachexia, may be said to correspond exactly and in every way with the classical symptoms of that disease; in other words, kala-azar is *primâ facie* malarial fever. And this view is further subserved by the fact that it exists in a region known to be malarious.

So cogent are these arguments, so close the similarity of the symptoms, that one might easily be tempted to declare the disease malarial fever without further preface—more so, perhaps, on actual view of the patients than from any written description. At any rate, the resemblance is so marked that until and unless malaria, as the cause of the disease, has been weighed and found wanting, it will be supererogatory to search for other factors.

But, it must now be carefully pointed out, a careful scrutiny of this kind is required before the malarial nature of the disease can be entirely accepted. In the first place, though this close resemblance exists, there are points at which the diseases appear to differ, and this has been felt so much that some people still cannot admit their identity. The high fatality of kala-azar, its intractability to quinine, and, above all, its communicability, have all been quoted as emphasising the difference; to these may, *perhaps,* be added the existence of a continued fever in the second stage of the malady.

Again, however close the resemblance of the two diseases as regards their grosser symptoms may be, the pathological anatomy and essential nature of the two may be quite different. Although it is certainly most improbable—to judge from our general experience in medicine—that two distinct diseases should produce a long train of identical symptoms, the thing is possible and must be guarded against.

For example, looking critically at the symptomatology, and remembering that the early days of the disease have rarely been studied by medical men, we may suggest that the clinical picture elaborated in paragraph 6 may not be quite correct in one particular—that the enlargement of liver and spleen may in fact *precede the appearance of the fever*—that this fever may in reality be not at all remittent or intermittent at first as supposed, but *continued* throughout, as it is later. Such a history, if it were the true one, would entirely disconcert the malarial theory, and would tend to exhibit the disease as primarily one of the spleen and liver accompanied by a secondary fever.

This view would be very compatible with the facts—supposing the history slightly changed as indicated. We might imagine almost any pathogenesis for the primary disease of the organs. We might conjecture the existence of a cirrhotic *foie infectieux*, and ascribe for it the pathogenesis which Adami gives of the Pictou cattle disease or something similar. Or we might attribute the local lesions to coccidia, which Giles says he finds frequently in the motions of cases of kala-azar [3, p. 19] and which may infect the organs; or to species of amœba coli or cercomonas, which I found in many of the cases and which we may easily conceive to permeate the organs; or to objects similar to those in the liver and spleen of birds, lately described by MacCallum [21], which he thinks may be some new protozoon, and which I too think I have recognised there; or

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to flukes of the organs, especially distomum sinense, which is known to produce in Japan a widely prevalent disease with enlargement of the liver and spleen, jaundice, anasarca and a final cachexia; or to some entirely new parasite, animal or vegetable. In such cases the fever would be of a secondary, possibly associated septic, nature—in which case we may even conjecture it, from our knowledge of septic fevers, to simulate quotidian intermittents.

Again, it may be quite possible that kala-azar is really akin to one of the primary anæmias—say Addison's Disease, Hodgkins' Disease or leucocythæmia. In these maladies we have anæmia, emaciation, often enlargement of the spleen or liver, and very frequently a persistent fever, closely similar to that observed in the second stage of kala-azar, and sometimes astonishingly like a malarial quotidian (the chronic recurrent fever of Ebstein). In Addison's Disease, moreover, there is a peculiar bronzing of the skin, which, translated to the native of India, may constitute the blackening popularly connected with kala-azar. It is true that those maladies are not known to be infectious, but a possibility of this remains open in the absence of more definite knowledge.

Lastly, as Dr. Manson has lately suggested to me, and as I have often thought in respect to some cases of paludism, we may, in such instances as occur in kala-azar, have an auxiliary bacterial invasion of the liver and spleen following a primary protozoal infection by the parasites of malaria.

Indeed, laying aside the apparent malarial pathogenesis of the disease, numerous suggestions may be made as to its nature; and it is obvious that a hasty conclusion based on its general similarity to paludism is not justifiable. I may now add that suspicions in this respect were violently excited in me by a discovery—to be related presently—which I made early in my pathological examination of cases of kala-azar; so that, on many grounds, it appeared absolutely necessary to undertake a careful examination of the question.

At the same time it was understood that if the disease proved to be malarial after all, further research as to its pathogenesis would not be required.

13. Literature bearing on the Malarial Nature of Kala-Azar.—In order to demonstrate the malarial nature of a given case of sickness, it is necessary not only to show the existence of occasional attacks of the typical fever, or the occasional presence of the typical parasites, or the typical enlargement of the organs, or even the typical pigmentation, but to establish that the *ensemble* of the symptoms accords with that of paludism. For instance, in a malarious country like Assam we may expect frequent attacks of fever in patients suffering from all sorts of diseases; we may expect even to find the enlargement and pigmentation of the organs in many. This is not enough. We require entire accordance, not only an occasional coincidence, of the symptoms.

Secondly, to establish an exhaustive diagnosis of paludism we must depend not alone on the macroscopic symptoms, but on a demonstration regarding the minute pathological anatomy, especially of the pathogenetic parasites, of their immediate product the black pigment, and of the remoter derivate of their toxic influence, the yellow pigment.

Whether this has been entirely done in existing literature on kala-azar is capable of discussion. So far as the symptomatology goes we have evidently a very clear accordance between kala-azar and paludism; but with regard to the minute pathology, it has been felt—see especially [14, p. 199]—that existing records are not complete.

Giles, proceeding on the ankylostomiasis theory, does not, naturally, examine the pathology closely from the malarial point of view. In the annual Sanitary Reports there is little reference to the histology; and the rest of the kala-azar literature depends for its facts in this respect on the report of Rogers. This report, then, practically constitutes the whole of the existing kala-azar literature relating to the pathological anatomy and histology. Captain Harold Brown's report [16] on kala-dukh, however, furnishes some valuable information which may apply to kala-azar.

It is necessary to examine the observations of the seofficers somewhat closely, as they differ materially from mine.

With regard to kala-dukh, Brown states that out of 50 cases of the disease examined by him he found the "hæmatomonas malariæ" in 45.

With regard to kala-azar, Rogers' observations are as follows. In his report [4, p. 116] he says, "the organisms were found in nearly all the more

advanced typical cases during the presence of fever, in all stages of the disease up to the day before death and in numbers roughly proportionate to the height of the fever." In his Reply to Criticisms [12, p. 249] he states still more definitely that "the plasmodium malariæ is constantly present in all stages of the disease." With respect to the pigment, he states, without specifying *which* pigment:—"It may at once be said that it was constantly met with in the series of cases (autopsies) examined, and that it was roughly in proportion to the chronicity of the case, being easily seen in properly prepared specimens in the more acute cases, while in the more chronic ones it was so marked as to be visible to the naked eye in thin sections floated out in a white vessel" [4, p. 111].

It will be confessed that if these observations are to be accepted, the malarial nature both of kala-dukh and of kala-azar must be taken as finally established. The discovery of the pathogenetic parasites and of their product, the black pigment, in so large a number of the cases, is a full complement to the presumptive evidence, already strong, based on the symptomatology of the disease. Here we have a train of symptoms, long and varied, coinciding exactly with those of malarial disease; and now, in addition, bodies so peculiar to paludism as the parasites are not only merely found in the cases (as Brown reports), but (as Rogers says) are present in all stages of the disease, and are even proportionate to the height of the fever, while the melanin so characteristic of paludism, is constantly met with in a series of autopsies. Not only are the parasites merely present, but they are present throughout the malady "up to the day before death," and are numerically in proportion to its severity. Admitting the facts, there can be no escape from the deduction. We have the symptomatological picture of an illness consisting of, first, attacks of high fever, secondly, enlargement of the organs, and, thirdly, cachexia due evidently to the enfeeblement or destruction of those organs; and at the same time we actually see the destructive elements, the parasites, at work at every stage of the disease, and find their excrementitious product, melanin, accumulated in the organs; we even have a coincidence between the number of the parasites and the height of the fever. No demonstration can be more complete: it is like the destruction of a piece of furniture by white-ants.

Whether, however, these observations are correct or not, it is incumbent on us here, as in all scientific work, to examine them closely. Unfortunately, Captain Rogers does not give us specific details sufficient to enable us to do this. His statements regarding both the parasites and the pigments are, in fact, astonishingly summarised and brief. Nowhere does he present us with a complete list of all the cases and autopsies examined by him, as Captain Harold Brown has done in respect to kala-dukh. As a matter of fact, he records notes of only twelve cases of kala-azar—and very brief notes. On examining these we find that the parasites were found only in five; while out of seven autopsies made on those of the twelve cases which died, the presence of pigment is recorded only in two, and then it is not specified which pigment is referred to. A temperature chart is affixed to only one case out of the twelve. Replying later to criticisms, however, Rogers [12, p. 250] explains that the reason why the parasites were found only "in five of the twelve clinical cases of which the notes were given, was simply because they only happened to have been looked for in those five out of that particular series." I can find no explanation in his writings of the absence of record of melanin in six of the autopsies—nor of the absence of charts. Further, there is no evidence recorded in this series of cases tending to prove the author's statements to the effect that the parasites are "constantly present in all stages of the disease," and that they were found "in numbers roughly proportionate to the height of the fever." All that is stated on those points is, in three out of the five cases in which the parasites were noted, that they were found when "his temperature was high" or when "he had fever;" and in the remaining two cases simply that they "were found in his blood this day"—apparently on a single occasion. These cases are seemingly given as exemplary cases of kala-azar, and it might fairly have been expected that in them, if nowhere else, the author would have recorded exact details to justify his very general and yet emphatic declarations respecting the presence of the parasites and the pigment in the disease. I should like to note, however, that on page 100 of his report he expressly apologises for not having been able to devote

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as much time as he could have wished to the microscopical part of the work, owing to the pressing claims of the epidemiology of the disease; the force of which will be felt by those who have had similar duties to perform.

Apart from these brief references to the parasites and pigments in the twelve cases, Rogers deals very curtly with this important part of the subject. With regard to the pigments, he covers all his own observations by declaring their coincidence with those of Kelsch and Kiener on paludism in general. He does not give his own experiences in regard to the amount and distribution of the pigments, and, indeed, does not refer to the yellow pigment at all, except indirectly in connection with some indeterminate estimations of iron in the liver of five cases. His statement quoted above, to the effect that "pigment" in the organs "was roughly in proportion to the chronicity of the case," would, if he refers only to the black pigment, be just the opposite of Kelsch and Kiener's observations (paragraph 27).

Similarly, he discusses the parasites only in two paragraphs of his report [p. 115] and in one paragraph of his Reply to Criticisms [p. 249]. He complains of a difficulty in studying the parasites in advanced cases of the disease in consequence of the anæmia causing "great changes in the sizes and shapes of the corpuscles." He gives no details as to the different forms of parasites met with, "except that in the kala-azar cases the organisms seemed to be less frequently pigmented"—without specifying what stage or form of the parasites he refers to. He observes no special variety in kala-azar, but says only that "the forms found include most of those figured by Italian authors as typical of quotidian fever"—adding, however, that he "never came across any crescent forms." He refers to having examined blood from the spleen during life, but gives no noteworthy details.

For my own part I must confess to a great difficulty in understanding the exact meaning of these statements. According to the Italian authors, quotidian fever is produced by all forms of the parasites of malaria—by a single generation of the quotidian parasite, by two parallel generations of the tertian parasites, or by three parallel generations of the quartan parasite. Hence there are no forms which can be said to be typical of quotidian fever—at least according to the Italian authors; and it is impossible to know which forms Rogers refers to. According to the Italians, moreover (and almost everyone else now-a-days), crescents are generally associated with the large group of æstivo-autumnal parasites, which certainly very frequently cause quotidian fever. The statement as to the deficiency of pigment in the organisms of kala-azar is, in absence of any more detailed specification of those organisms, too vague to be easily comprehensible; and it is difficult to grasp how changes in size and shapes of the corpuscles can make a study of the enclosed parasites materially more difficult.

I have criticised Rogers' statements in these respects somewhat narrowly, not only because they differ from my own observations, but because they refer to a point of great importance in regard both to the nature of kala-azar and, I think, to its treatment. To sum up, I believe it will be felt that his observations in regard to the parasites and pigments are not given in sufficient detail to establish entirely the malarial nature of kala-azar—certainly not to justify the neglect of further investigations.

In this connection there is on record a remarkable case, said to be of kala-azar, taken by Dr. J. B. Gibbons, and read before the Calcutta Medical Society in 1889. The case was one of enlargement of liver and spleen, fever, emaciation and some dysentery, the illness being of a year's duration. It is transcribed fully in Appendix B. Gibbons calls the case Assam fever, probably kala-azar, but, unfortunately, does not mention where precisely the disease was contracted. It will be seen that the case reads exactly like my clinical picture of kala-azar between the second and third stages. There is not only the enlargement of the organs, but the constant low fever referred to by me. Death seems to have occurred in consequence of intercurrent dysentery with high fever. At the autopsy Gibbons states expressly twice that there was no pigmentation of the spleen; but there were minute masses of brown pigment in the hepatic cells. He draws the distinction between this case and instances of malarial poisoning in Lower Bengal, where he says the spleen always contains large quantities of pigment.

I shall refer later (paragraph 31) to Brown's pathology of kala-dukh, but may state here that crescents were found by him in 43 out of the 50 cases noted.

It is necessary now to mention briefly some of my own experiences in these respects—the details will be given presently (paragraphs 17 and 18). Judging from Brown's and Rogers' reports, I expected to find the parasites readily in most cases of kala-azar; and I felt that if this were the case the nature of the disease would scarcely require further discussion. When I arrived at Nowgong there was a group of cases in the Civil Hospital there, all of which had been diagnosed kala-azar by Captain McNaught, and all of which presented the typical symptoms of that disease of the second stage. The livers and spleens were always greatly enlarged, there were various degrees of anæmia and emaciation, and occasionally dropsy of the feet, and most of the cases were suffering from constant fever. The pathological examination gave the following results:—

(*a*) Not a single malaria parasite could be discovered on repeated and careful examinations of the peripheral blood in the large majority of the cases, even when fever was present (as was almost always the case).

(*b*) Examination of blood taken from the spleen, and sometimes the liver, during life, showed the presence neither of parasites nor, in most cases, of the black pigment.

(*c*) In two out of seven autopsies made on cases which had been diagnosed kala-azar by Captain McNaught, neither parasites nor black pigment could be found in the spleen and liver.

(*d*) Careful thermometric observation of the patients showed that the temperature charts gave the curve of constant low fever, and not of typical malarial fever of any kind.

(*e*) The yellow pigment was present in the liver in all the autopsies but one, and was extracted from that organ during life in some of the cases.

I am not prepared to say that the parasites and black pigment were entirely absent in those cases—such can never be said with confidence in regard to patients living in malarious localities; but I will say that, if present, they were so scarce that they could not be detected even after very careful search, and that they must have existed in almost infinitesimally small quantity as compared with the quantity in which they are found in ordinary recent malarial infections.

These results, then, raised a very grave suspicion that kala-azar, in spite of its great clinical similarity to paludism, was really something quite different.

It was necessary to make a closer examination of the question.

14. The Special Pathological Problem Presented.—Either kala-azar is not malarial fever, or it is so, *in spite of the frequent absence of parasites and black pigment in one stage of the disease.*

Just as it would have been rash to assume the malarial nature of the disease on the strength of the symptoms alone, so now it might be equally unpermissible to reject this pathogenesis on the grounds I have given.

If kala-azar be malarial, and if my observations be sound, it will follow that the parasites and pigment may be absent at a certain stage of a malarial infection. Now it may be taken as granted on the authority of every competent observer that the parasites are present at least in the beginning of every case of paludism; and it is generally held that in most cases, if not in all, there is pigmentation of the organs. How then account for their absence in these severe cases—at a time, too, when the fever and the general condition of the patients showed that a morbific agency, whatever it is, was most certainly at work?

There is this possible explanation—that kala-azar is malarial fever in which the original violent parasitic invasion gradually dies out during the first stage of the disease; leaving in the second stage an acute tumor of the spleen and liver, accompanied by a constant secondary or symptomatic fever; and finally resulting in a cachexia in the third stage. It would be possible to conceive that the black pigment is eliminated shortly after the disappearance of the parasites, leaving, however, the surcharge of yellow pigment actually found at the autopsies.

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But this hypothesis cannot for a moment be submitted to, unless we can find sufficient evidence in fact and sufficient authority in literature to favour it.

In the meantime, I propose to employ it merely as a useful working hypothesis for the better classification of observations.

I shall begin, then, with an exhibition of such facts as I could collect in the brief period allotted to the work ; and shall then proceed to a theoretical discussion of obscure points.

15. Mode of Investigation Adopted.—Had it been possible to examine a number of cases of undoubted kala-azar from start to finish, the enquiry would have presented less difficulty. As pointed out in paragraph 7, however, medical men familiar with the disease are unwilling to give a definite diagnosis of kala-azar in its earlier stages. It cannot well, then, be studied in its earlier stages. There will always be the danger that any particular case of recent fever may ultimately turn out not to be kala-azar at all. Now by the hypothesis on which we are working, it is just in these early stages, and only in them, that we may expect to find parasites and black pigment.

I had hoped to be able to overcome this difficulty by studying the disease in a village recently and severely attacked ; but the same obstacle will present itself here. In such a village we should certainly find many recent cases of fever mingled with old cases of kala-azar ; but how be assured that the recent cases are in the early stage of kala-azar at all, and not in that of the ordinary malarial fever which abounds everywhere in Assam ? Nothing might be more misleading than conclusions founded on such observations—unless the observations were protracted over a long period ; they would rightly be challenged at once on the ground of this ambiguity.

Rogers has described this difficulty excellently in his report [page 25 *et seq.*]. The method adopted by him was to examine a number of cases of early fever and then to return to them a month or six weeksl ater, noting those which had developed more marked symptoms of kala-azar in the meantime. For me, however, this required more time than could be conveniently spared; and was, besides, open to the objection that the cases which ultimately proved to be kala-azar may have contracted the true infection, on the top of an attack of ordinary fever, in the interval.

On the whole, the course, which promised to be most instructive was the simplest one. It was to sit down in a large village or town where cases of kala-azar were occurring at the time, and to examine there all cases of fever of every kind which could be procured, comparing the *ensemble* of the clinical and pathological facts obtained. The town of Nowgong, where numbers of instances both of recent fever and of established kala-azar were to be found in proximity to the Civil Hospital, was admirably suited to the purpose. The Hospital was popular and was attended daily by many out-patients ; the in-patients remained willingly ; and autopsies were procurable.

16. Remarks as to the Cases Examined.—Every case of fever or kala-azar examined by me, however briefly, will be entered in the following list. My reason for doing this is to permit a judgment being formed on the evidence, independently of any opinion of mine.

Many of the cases being out-patients were observed but once ; others were refractory to examination ; others were so dull that I considered their evidence as to their history not fit for record ; others again could be dealt with only very hurriedly under pressure of the labour entailed by the necessary re-examinations of other patients. Many cases which I should like to have considered were abandoned altogether for want of time ; so that the total number is not large, while in many instances the notes are very short.

While engaged upon the work it was necessary for me to examine daily a large number of mosquitoes in connection with my other duties in respect to malaria, as explained in paragraph 1. This compelled me to confine myself to the essential details of the cases, and to exclude reference to such secondary symptoms as did not vitally concern the questions under consideration.

The points recorded were, the duration of the illness ; the history where reliable ; the presence of the parasites and their varieties, and of the pigments ; the temperature when it could be taken ; and the condition of the spleen and liver.

The blood was searched for parasites in every case but two. In many of the out-patients I was able to make only one examination; but that was always a very careful one, especially if the parasites were absent or scarce. I employed the classical unstained mode of preparation as being generally enough for diagnosis. This is quite sufficient for the detection of all the older parasites, but, as Marchoux points out [22, p. 6], the smaller unpigmented forms are so transparent that they often escape detection unless coloured. Hence, in many of the examinations I employed also a method of wet-staining with Loeffler's blue for the purpose. A minute drop of blood is taken up on a cover-glass and is placed in the middle of a small drop of the stain placed on the slide. If done skilfully this gives a very beautiful demonstration. Comparison with an unstained liquid preparation of the same blood confirms Marchoux's observations, and shows that the youngest amœbulæ, especially of the æstivo-autumnal varieties, are seen much more readily in the stained specimen. All the same I find no difficulty in detecting those parasites by the usual method. The pigmented organisms can, of course, be seen at a glance anywhere.

In cases where the parasites or pigmented leucocytes could not be discovered after one or two examinations of the peripheral blood, recourse was had to the spleen or liver, if the patient allowed it. A stout hypodermic needle, kept free from rust in oil and sterilised before use, was inserted into the organ and then twisted and slightly withdrawn, so as to encourage the entry of some of the hepatic or splenic cellular tissue with the rush of blood. If this failed, a second or third puncture, combined with haustellation by means of syringe, was had recourse to. It is absolutely necessary to obtain some of the parenchymatous substance for these observations, particularly because the yellow pigment is contained only in it; but in some cases I failed to secure it, owing to the rush of blood into the needle from the highly congested organ. In some cases, moreover, I could obtain no tissue nor even blood, even after several punctures. If the first puncture failed there was always the danger that the patient would refuse to permit a second. Nevertheless, success was generally obtained. The blood and tissue thus procured were entirely used up in making numerous specimens, stained or unstained, and of various degrees of thickness, for the detection of pigment in the mass; and all these specimens were invariably searched exhaustively. I never observed the slightest ill-effect from this operation.

The out-patients were examined as frequently as I could persuade them to come to hospital. Observations of the in-patients were made more regularly.

The temperatures of the out-patients were generally taken only during examination, the hour being noted. In some cases, however, reliable sections of charts were obtained. The charts of the in-patients were recorded by Hospital Assistant Ashab Ali, whose services were very kindly placed at my disposal by Colonel Calthrop, Principal Medical Officer of Assam. His thermometry is to be relied on, as I took every precaution that it should be so. I did not think it advisable to attempt nocturnal temperatures, as they were not absolutely necessary and there were obvious difficulties in the way of checking them.

In the autopsies, as in other observations, I was obliged to confine myself to the leading features—chiefly to the pigments. The human body is such an enormous organism that anything like an exhaustive survey of the pathological anatomy and histology is almost an impossibility to a single observer, especially when he has to deal with numerous other cases on the day of the autopsy.

All the patients, except Case 66, were poor people—mostly inhabitants of Nowgong.

The cases are generally arranged in an order depending on the duration of the illness; but this principle has been departed from in Cases 16 and 17, which belonged to the same family, and again in Cases 18, 19, 20, 21 and 22, for the same reason. I have also grouped together, near the end of the list, a series of in-patients suffering from well-established kala-azar, whose temperature charts are given in Appendix C, and have collected similarly the group on which autopsies were performed.

It should be understood that, while the duration of the illness can be ascertained with something like certitude from the patients when the illness is a recent one, it is impossible to do so in old cases. In such we must content ourselves with a rough record of months or years.

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17. Cases of Fever examined at Nowgong.—

Fifty-Four Mixed Out-Patients.

Case 1.—Hemaconta, m., 28, policeman of Nowgong, 2 days ill. Was taken ill on 15th September with very high fever and was brought to hospital in an unconscious state. Examined 17th; 9 A.M., just recovering from pernicious cerebral access. Temperature 101·6° F. Condition of spleen and liver could not be clearly ascertained, but no marked enlargement, no anæmia nor emaciation. Peripheral blood, only one mature quartan parasite after long search. Examined again at 3 P.M. and at 9 A.M. on 18th; no parasites found. Complete recovery from 17th; no ensuing enlargement of the organs. Quinine.

NOTE.—Pernicious access with quartan parasite found.

Case 2.—Mola Bux, m., 5, 3 days ill. His father says that he lost four sons, brothers of this child, from kala-azar three years ago, and that people in his house frequently get fever. The child was attacked with high fever with rigors on 16th September. Examined 19th; temperature 101·4° F.; looks very ill, already somewhat anæmic. No enlargement of the organs. Well nourished. Fever continuous since attack. Peripheral blood, 8 A.M., numerous small unpigmented amœbulæ, frequently assuming ring forms (æstivo-autumnal). No pigmented leucocytes. No larger parasites, many doubly-infected corpuscles. Quinine given; seen again 3rd Oct. Father says he has had no fever since last seen. Looks recovered but very yellow. Spleen 2 inches below ribs, and liver distinctly palpable and evidently tender. Temperature 98·2° F., 8 A.M. Peripheral blood, no parasites, no crescents. Temperature was taken by A. A. for a week after this date, and varied irregularly from 97·3° to 99·1°F. Quinine given steadily. Recovery; decrease of organs; no crescents on several examinations.

NOTE.—Rapid enlargement of organs and absence of crescents.

Case 3.—Budu, m., 35, 5 days ill. No reliable history; says fever irregular with rigors. Examined 1st Oct., 10 A.M. Looks ill. Peripheral blood, fairly numerous small quartan parasites, one mature one; no enlargement of spleen, nor of liver; not seen again.

Case 4.—Sorab Ali, m., 8, 5 days ill. Father says several of his children died some years ago with kala-azar. This child was taken ill five days ago with dysentery followed by fever, no rigors. The fever remains continually slight; dysentery is now better. Examined 1st Oct. 11 A.M. Anæmic, but not particularly ill. Temperature 101·4° F. Peripheral blood, no parasites nor pigmented leucocytes. The temperatures were taken by A. A. for 12 days from this date and remained between 98·2° and 99·2° F. Peripheral blood, frequently examined up to 20th October, never showed parasites nor pigment. Patient played in streets and was not ill. No enlargement of the organs was ever noted; motions tended to be loose but were never brought for my examination.

NOTE.—Nature of case indeterminate, slightly raised temperature and no enlargement of the organs.

Case 5.—Moshan, m., 45, out-patient, 5 days ill. Says had fever on two days, with two days free between; came yesterday; begins at 4 P. M., with rigor. No reliable history of sickness in his house. Examined 4th October 10-30 A. M. Looking rather ill, but no enlargement of the organs, nor anæmic. Temperature 98·0°F. Peripheral blood, one young quartan parasite found after a considerable search. Came into hospital; quinine; complete recovery forthwith.

Case 6.—Khoru, m., 2, 5 days ill. Mother says was attacked with severe fever 5 days ago, which has continued every day since with slight morning remissions only. No relatives are now getting fever. Examined 10th October 10 A.M., child ill and crying; already somewhat anæmic. Temperature 99·2°F. Spleen palpable; enlargement of the liver can just be felt. Peripheral blood, one full-sized and one medium sized tertian parasite; a crop of unpigmented amœbulæ forming rings—young of the æstivo-autumnal parasite; parasites not very plentiful. Examined again on 11th, 7.30 A. M. Mother says had high fever last night. Tertian parasites of all sizes; no æstivo-autumnal parasites. Quinine; recovery forthwith; no subsequent enlargement of organs.

NOTE.—Early enlargement of organs with two species of parasites.

Case 7.—Bahadur, m., 30, 6 days ill. Says was attacked 6 days ago. Came to hospital on 13th September with fever. No fever on 14th until evening. Quinine. Examined 15th. Looks rather ill; no enlargement of organs. 4 P. M., temperature 99·6°F. Peripheral blood; no parasites, one pigmented leucocyte. 16th, one amœbula. Recovery forthwith; no subsequent enlargement of organs.

Case 8.—Bikir Ram, m., 10, 6 days ill. Father says fever begins daily with severe rigor, and becomes very high. No relatives have had fever or kala-azar. Examined 18th October. Looks very ill already and is groaning with pain; cannot stand; complains of great pain in epigastrium. Spleen an inch and a half below ribs, not tender. Liver half an inch below costal arch and tender. Father says, had slight fever four months ago, but it left no enlarged spleen; 9 A. M. temperature 103·3° F. Peripheral blood, no parasites nor pigmented leucocytes. Examined again at 2-30 P.M.; father says the fever has been continuous since yesterday, but there was a shivering fit at 10 A.M. (after previous examination). Temperature 103·3°F., is now perspiring freely and looks somewhat relieved. Peripheral blood, numerous unpigmented amœbulæ [æstivo-autumnal], with "tongues" (paragraph 21). Pigmented leucocytes. Large doses of quinine. Examined again on 20th; 8 A. M., temperature 99·1°F. Feels much better.

Spleen and liver noticeably larger than on 18th. Boy says now that both are tender. Peripheral blood, one æstivo-autumnal amœbula. Not examined again.

NOTE.—Rapid enlargement of the organs, especially liver; and tenderness in the latter.

Case 9.—Metabadal, m., 30, from distant village, ill about six days. Says almost continuous high fever with rigors. Examined 18th September. Looks ill; high fever all day; old enlarged spleen; no appreciable enlargement of liver. Temperature 102·8°F. at 5 P.M. Peripheral blood, several tertian parasites of different generations; numerous small amœbulæ, unpigmented, forming rings, some in small dark green corpuscles; one nearly mature æstivo-autumnal parasite—a mixed infection. Admitted; quinine. Re-examined 21st September, much better; no parasites. Recovery forthwith; no decrease in spleen.

Case 10.—Bharu, m., 10, 10 days ill. Boy says his fever comes one day on and two days off. No history respecting relatives recorded. Examined 1st October morning. Says fever began this morning with rigor which is just passing off. Looks ill and half-starved, but not emaciated; considerably anæmic. Spleen one inch below ribs; liver one inch below ribs and tender. Declares repeatedly that he has had no fever for years until this attack ten days ago. Temperature 103·4°F. Peripheral blood, one full-sized quartan parasite, and a few medium-sized; no pigmented leucocytes. Blood from spleen, numerous quartan sporulating forms and a few half-grown parasites. Spleen cells procured; they contain a small quantity of melanin—clumps up to 3μ in diameter, and clusters of oscillating isolated granules. A few granules in every field—melanin by no means copious. No yellow pigment found. Quinine regularly. Examined again 11th October. Says no fever since he last saw me. Enlargement of spleen has entirely disappeared, but liver still remains enlarged one inch below ribs. Patient says, however, that it is no longer tender. Blood not examined, not seen again.

NOTE.—Rapid enlargement of organs and persistence of liver enlargement after disappearance of splenic tumour. Also large number of quartan sporulating forms in spleen when none were found after careful search in peripheral blood, also small quantity of melanin in splenic cells, even at height of illness.

Case 11.—Molo, m., 35, 11 days ill. Says fever began with rigor 11 days ago, since when it has been continuous with only morning remissions. Examined 19th October, 11 A.M. Temperature 101·5°, rigor just beginning, no enlargement of liver or spleen. Does not look seriously ill. Peripheral blood, one crescent, becoming flagellate, after careful search; no other parasites. Not seen again.

NOTE.—Absence of enlargement of organs and of apparent illness of patient.

Case 12.—Iarbee, f., 6, 12 days ill. Mother says fever is continuous. There were kala-azar cases in the house a year ago. Examined 24th September at 10 A.M., slightly anæmic and looking rather ill. No emaciation or enlargement of spleen or liver. Peripheral blood, no parasites or black pigment, numerous leucocytes. Temperature 100° F.; seen again on 16th October; liver one inch below ribs; spleen palpable; blood could not be examined. Father says no fever for a fortnight; much better.

Case 13.—Ramchandra, m., 10, out-patient, 15 days fever. Says he has fever every third day, severe, with rigor, comes regularly (information volunteered). Examined 30th September at 7-30 A.M. Temperature 97·4°F. Looks ill; spleen palpable under the ribs; no appreciable enlargement of the liver. Peripheral blood, numerous medium-sized quartan parasites, one generation; pigmented leucocytes. Splenic blood; spleen-cells contain melanin in every field from smallest grains to large agglomerations. The (medium-sized) parasites are not more numerous in the splenic than in the peripheral blood. No yellow pigment; more pigment than in Case 10. Not seen again.

NOTE.—No hepatic enlargement.

Case 14.—Silahin, m., 40, 20 days fever. Has lately had severe fever, apparently of tertian type, with rigors for 20 days, not longer. Is now better, looks pale but not ill. Not emaciated. Spleen four inches below ribs. No enlargement of liver. Examined 19th September at 9 A.M.; temperature 97·6°. Peripheral blood, a very few æstivo-autumnal amœbulæ, not pigmented; a pigmented leucocyte. Again at 5 P.M., three amœbulæ as before; one crescent after long search. Examined frequently, one or two crescents found occasionally; but not always, very rare. Says slight fever occasionally; quinine regularly. Not ill; does hard work. On 4th October spleen had almost disappeared. No hepatic enlargement. Peripheral blood, one crescent. Splenic blood, numerous spleen-cells, almost all of which have masses of melanin from smallest granules to large agglomerations; no crescents found here. No yellow pigment noted.

NOTE.—Large amount of melanin in spleen.

Case 15.—Kaila Din, m., 11, 20 days ill. No history recorded. Examined 24th September at 3 P.M. No enlargement of the organs; slight anæmia. No fever now. Peripheral blood (hasty); no parasites. Not seen again.

Case 16.—Bang, m., 25, 20 days, ill. Says was taken ill with severe fever with rigors 20 days ago, some weeks after his step-mother, Dipkalia, the next case, who lives in the same house; after lasting 10 days, the fever has nearly left him, but he still feels it occasionally. Examined 24th September, 8 A. M., temperature 98·4°F. Is no longer ill, but considerably anæmic and quite yellow. No enlargement of the spleen and liver apparent; strong young man. Peripheral blood; fairly numerous, rather large aestivo-autumnal unpigmented amœbulæ; one pigmented leucocyte. The amœbulæ have "tongues" (paragraph 21). No crescents after careful search. Quinine. Examined again on 29th September, 9 A. M., temperature 99·0°F.

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Says no fever since the 24th. No enlargement of liver and spleen. Peripheral blood, no parasites, nor pigmented leucocytes; no crescents. Examined again on 18th October. Has been taking quinine and says he has had no fever since I saw him. There is no enlargement of the organs, and the blood contains no parasites or melanin. Is no longer anæmic and looks quite well.

NOTE.—No enlargement of organs and no crescents. A pigmented leucocyte was found with the amœbulæ on the 24th, showing presence of melanin somewhere.

Case 17.—Dipkalia, f., 18, out-patient, one and a half months ill (entered here as she is step-mother of the last case, and was taken ill about three weeks before him). Fever very severe, with rigors. Still gets it daily. She and her step-son say that no people died of kala-azar in their house, and other inmates are not getting fever. Examined 24th September, 7-30 A. M., temperature 102·4°F. Looks extremely ill and of a pale yellow; is hardly able to walk; complains of pain all over the body and especially in epigastrium. Has become quite thin. No œdema of feet. Spleen only just palpable below ribs as a small tumor, but the liver extends to two inches below the costal arch and is certainly very tender. Peripheral blood, numerous large unpigmented æstivo-autumnal amœbulæ with "tongues"; pigmented leucocytes; no crescents at all. Quinine in large doses. Seen again on 27th, 9 A. M., temperature not recorded. Says fever better, but looks extremely ill and can only just walk. Peripheral blood, a few large unpigmented amœbulæ with "tongues;" one of the largest of these, however, contains a few minute granules of pigment; no crescents. Splenic blood, cells obtained, fairly copious melanin, some in every field; no crescents; pigmented sporulating and full-grown forms precisely similar to Malchiafara and Bignami's æstivo-autumnal tertian—that is, largish parasites with an undefined margin, containing a central clump of melanin and producing a few rather large spores (paragraph 21). The smaller parasites have a few small granules, as found in the finger-blood. There are two generations present, but there is considerable graduation of sizes. Examined again on 29th, 8. A. M., temperature 97·2° F. Says she has noticed no fever since I last saw her 27th. Peripheral blood, a pigmented leucocyte; no amœbulæ; no crescents. Looks a little relieved. The senior Hospital Assistant of the Civil Hospital, who is very familiar with kala-azar, thinks the case may be one of that disease, but is of opinion that the spleen and liver should have enlarged more by this time, as the patient has been ill for a month and a half. Quinine regularly in large doses. Examined again on 30th. Peripheral blood, no parasites. Looks very ill, but says no fever; temperature 97·0° F. at 9 A. M. Enlargement of spleen and liver just as before. On the 4th October there was a marked improvement; patient was rapidly regaining strength and colour, and said there had been no fever at all. Tumour of organs has decreased rapidly; spleen can no longer be felt at all, and liver is only just palpable. Says is pregnant, and refuses to take quinine; a decoction of cinchona ordered. On the 19th October was seen for the last time. Was very much better, but still rather weak and anæmic. Spleen not enlarged, but liver still noticeably so, and is still certainly tender. Says no fever for a long time. Taking the decoction. Splenic blood, copious parenchymatous tissue obtained; not a single parasite, even a crescent; *not a single particle of melanin.* No yellow pigment found. Not seen again.

NOTE—This and Case 16 occurred in the same house one after the other, and contained evidently the same parasite. It is remarkable that no crescents were found in either case. In spite of the serious nature of the attack, especially in Case 17, the organs, particularly the spleen, were not affected to a great degree. Fairly copious melanin found in spleen on 27th September; none on 19th October.

Case 18.—Assir-u-din, m., 6, one month ill. This and the next four cases belong to the same family. From careful enquiries of the parents it appears that that they had nine children, of which four have died. One died of kala-azar three years ago; two of "fever" and one of "headache" about a year ago. Then the father and four of the remaining children were attacked with fever one after the other, the mother and one child escaping hitherto. The first attacked was Amir-u-din (Case 22), a year ago; then the father, Bassur-u-din (Case 21), and another child, Ramad Ali (Case 20), both two months ago; lastly this case and Saffir-u-din [Case 19], one month ago. The exact dates are not very reliable. Parents say that their child who died of kala-azar had symptoms exactly like these surviving children, but that in his case there was an extremely severe recurrence of fever after a month from the beginning of his illness, from the effects of which he finally died. They add that in all the cases the illness begins with continued fever for ten days or so, with numerous severe rigors. The fever then gradually subsides, leaving enlarged spleen, but recurs frequently at various intervals. For some time past the present child (Case 18) has been getting fever with rigor every third day. Examined 7th October, 9 A.M., temperature 97·8° F. Looks extremely ill; is of a yellow colour and very anæmic; depressed expression; no œdema; no emaciation. Spleen 3 inches below ribs and liver one inch (patient being a small child); both tender on pressure. Several Hospital Assistants familiar with kala-azar think that this case and Cases 19 and 20, and possibly 22, are very probably cases of commencing kala-azar. Peripheral blood, numerous quartan parasites of two generations; some nearly mature, others a day younger. Many of them are contained in small dark green corpuscles. The youngest parasites have very rapid amœboid movements for quartan parasites, and pucker up the corpuscle as they change shape. Examined again on 8th October, 9-30 A.M., temperature 96·9° F. Peripheral blood, same parasites as yesterday; one parasite on the point of forming nine large spores. Quinine. Seen frequently again up to 19th October. Fever and parasites disappeared rapidly, but the enlargement of the organs abated but little.

Case 19.—Saffir-u-din, m., 4½, one month ill. Brother of above, and parents say gets the same kind of fever, but has slight dysentery and diarrhœa as well. Examined 7th October,

10 A.M., temperature 98·4° F. Does not look as ill as last case; is cheerful and fat, though anæmic. Spleen and liver both one inch below the ribs and tender. Peripheral blood, exactly the same parasites as last case, but only one half-grown generation in dark green corpuscles, which they pucker as they move; less numerous. Quinine. Seen frequently. Improved gradually; enlargement of spleen gradually almost disappeared, but that of liver remained.

Case 20.—Ramad Ali, m., 11, two months ill. Brother of above. Says fever, which was formerly continuous, now comes every third day. Examined 8th October, 9 A.M., temperature 97·9° F. Boy says he had fever yesterday. Does not look very ill, and is not emaciated or œdematous; but is of a yellow colour and considerably anæmic. Spleen 2 inches and liver half an inch below the ribs; both tender. Peripheral blood, no parasites nor melanin. Examined again on 9th October, 8 A.M., temperature 97·7° F. Boy insists that he had fever on the 7th at 2 P.M., and that it left him at 4 P.M.; and adds that it will come on to-morrow at about the same time. Peripheral blood, one single medium sized quartan parasite rapidly amœboid for quartan, in a dark green corpuscle. No other parasite found. Improvement under quinine as last cases.

Case 21.—Bussor-u-din, m., 50, two months ill. Father of the last three cases. Says he gets fever only occasionally now, and that he has not had it lately. Begins with rigor. Examined on 8th October, 8 A.M., temperature 97·7° F. Spleen 4 or 5 inches below the ribs, not tender. No enlargement of liver. Looks nearly well. Peripheral blood, no parasites nor melanin. Not examined again, as he had no more fever after taking quinine. Spleen was little reduced in size on the 19th October.

Case 22.—Amir-u-din, m., 2½, one year ill. Son of last case and brother of the three preceding cases. Had severe fever formerly, but has been better for a long time, though he still has slight fever. Father says his spleen was formerly greatly enlarged. Examined on 8th October, 10 A.M., temperature 99·7° F. Looks anæmic and slightly ill. No enlargement of spleen, but liver is palpable. Peripheral blood, no parasites. Examined on several future occasions in the morning; the temperature was always found to be between 99° and 100° F., and no parasites or pigment were observed in blood. Spleen not permitted to be examined. No change on 19th October.

NOTE.—This family of five persons is interesting. The same parasite was found in three of the earlier cases, accompanied by considerable enlargement of the organs, the general condition of these cases approaching that of established kala-azar. In the first cases the morning temperature was generally subnormal and the fever was easily affected by quinine. In the last case (of a year's duration), however, the morning reading always showed a slightly raised temperature, suggesting a continuous fever; and this fever remained entirely unaffected by quinine.

Case 23.—Sadur, m., 12, one month ill (?). Comes from Roha, where there has been much kala-azar (paragraph 5). Says father and mother died of fever (? kala-azar). Says he has had fever for one month, but this statement is not reliable. States that the fever comes every other day with shivering (information volunteered) at about 2 P.M. Examined on 22nd September at 8-30 A.M., temperature 98·4°. Does not look very ill; considerably anæmic; no œdema; spleen nearly to umbilicus; lower edge of liver half-way between lower end of sternum and umbilicus (much enlarged). Peripheral blood, a leucocyte containing spring tertian pigment, a large spring tertian parasite and small unpigmented amœbula—nothing else. Splenic blood; numerous spleen-cells. A cluster of black pigment in a spleen-cell in about every four fields; pigment not at all copious. Numerous parasites having the appearance of red corpuscles containing several large rounded grains of black pigment, the plasma of the parasite being extremely undefined—like æstivo-autumnal tertian parasites, nearly mature (paragraph 21). No yellow pigment found. Few spring tertian parasites here. Patient not seen again.

NOTE.—The duration of this case appears to be more than one month. There are two varieties of parasite present. Thought to be possibly kala-azar.

Case 24.—Bhawan, m., 35, one month ill. Says fever comes every evening. Examined 26th September, at 10 A.M.; temperature 97·4° F. Not at all ill, but anæmic. No emaciation or œdema. Spleen approaching umbilicus; liver not enlarged. Peripheral blood, two æstivo-autumnal amœbulæ in one corpuscle; nothing else, 3 P.M., one similar amœbula; no fever. Not seen again.

Case 25.—Bhorali, m., 15, one month ill. Says fever comes every other day or every third day, with rigor. Examined 4th October, morning; considerable anæmia and emaciation; no œdema. Spleen 2 inches below ribs; liver just palpable. Peripheral blood, a few typical quartan parasites, some within small dark green corpuscles. Patient not seen again.

Case 26.—Mahomed Ebrahim, m., 25, one month ill. Says he caught fever from his son. No kala-azar in his house. Examined on 24th September at 3-30 P.M., temperature 99·5° F. Not looking ill; no anæmia. Liver not enlarged, spleen 4 inches below ribs. Fever just beginning with rigor. Peripheral blood, no parasites or pigment. Examined again next morning; one doubtful ring form (æstivo-autumnal) in blood. Spleen pricked on 17th October; no blood obtained. Not seen again.

Case 27.—Koram Ali, m., 9, one month ill. Is well-known in the hospital. His father and sister died of kala-azar a year ago, and his mother now has it, but is better. Severe fever began a month ago, lasted ten days and then stopped; came on again yesterday. Examined 1st October, 10-30 A.M., temperature 99·8° F. Looks ill and yellow; anæmic; no emaciation Spleen 2 inches below ribs; liver not enlarged. Peripheral blood, no parasites. Examined again on 3rd and 4th October. Spleen increased to three inches below ribs; blood, no parasites. Temperatures taken twice daily showed a high continued fever from 100·5° to 104·2° F.,

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lasting for a fortnight. Was examined again on 15th October and was found to have pleuro-pneumonia on the left base. Had become very ill and was unable to walk; very anæmic and considerably emaciated. Spleen more than 4 inches below ribs and liver 1 inch; both very tender; high fever. Hospital Assistants think the case is kala-azar; Captain McNaught thinks it may be so. Peripheral blood, no parasites. Splenic blood; numerous spleen-cells obtained, many of which contain black pigment, while others contain yellow pigment. The melanin is in small granules, scattered singly or numerous in the cells. No agglomerated masses larger than 3μ in diameter. It is not copious. The yellow pigment is in characteristic, small, angular, bright-yellow granules within isolated cells; much less abundant than the black, and does not blacken with ammonium sulphide. No parasites at all found. The patient had been taking quinine regularly. Improvement followed from this date to the 20th October, when I last saw him.

Note.—Sufficient search for parasites was not made in this case at the beginning of the second conflagration of fever occurring on 30th September; but the splenic melanin; which had every appearance of being recent (and, I think, belonged to the quartan parasite), proved the presence, at least lately, of a parasitic invasion. The high continued fever was probably partly due to the pleuro-pneumonia, but the extreme tenderness of the liver and spleen almost suggested an inflammatory condition in them also. Note also the presence of yellow pigment and rapid enlargement of the organs.

Case 28.—Nur Baks, m., 30, one month ill (?). Says that two men died of kala-azar in his house a year ago, examined 8th October. Liver 2 inches below ribs. Spleen to umbilicus; both tender. Does not look at all ill, but is a little anæmic. Peripheral blood, no parasites or melanin. Not seen again.

Note.—The case is probable of longer duration than one month.

Case 29.—Gubinath, m., 18, one month ill. Says his fever is continuous, but that rigors occur. His mother died of kala-azar five years ago, and his uncle has been having fever for four months. Examined on 10th October, at 7-30 A. M.; temperature 97·5° F. Looks ill; considerable anæmia and some emaciation. Spleen three inches below ribs; liver not enlarged. Peripheral blood, numerous tertian parasites of two generations. They contain particularly fine pigment of a very light colour (paragraph 20). Quinine. Seen again on 12th; temperature 95·8° F. Says fever has left him. No parasites. Recovery. Spleen remained enlarged to 20th October.

Case 30.—Nial, m., 45, one and a half months ill. Says fever is irregular, with rigors, and that he is now better. Examined on 3rd October, morning; temperature 98·2° F. Does not look ill. No œdema or emaciation; but marked anæmia. Spleen 3 inches, and liver 1½ inches below ribs. Peripheral blood, no parasites nor melanin. Seen on 17th October; the spleen was found to have decreased to 2 inches below ribs, and the liver increased to 2 inches. Says he has been having no fever lately after taking quinine. Blood not examined.

Case 31.—Kandura Riot, m., 25, policeman, one-and-a-half months ill. Says fever comes with rigor, lasts six days or so and then remits for about three days. Examined 4th October, morning. Temperature was 103° F. last evening, and is 99°F. this morning; very slight anæmia; looks not very ill. Peripheral blood, one small unpigmented æstivo-autumnal amœbula only. Spleen 3 inches and liver ½ inch below ribs; both tender. Spleen pricked, but no blood obtained. Not examined again. Recovery.

Case 32.—Amiran, f., 10, 2 months ill. Says she gets fever every three days with rigor. Is well known. No one in her house is now getting fever. Examined 20th September, at 9-30 A. M.; temperature 97·6°F. Looks considerably ill, but is not very anæmic; emaciated. Spleen 3 inches and liver 2 inches below ribs; tender. Peripheral blood; a few quartan parasites, many in small, dark green corpuscles; only one generation. Was watched for some weeks, the blood being frequently examined. The fever occurred with exactness every third day and parasites were constantly present; being little influenced by quinine, which, however, was not taken regularly. Typical quartan sporulating parasites were occasionally observed in the peripheral blood. There was practically no change by the 20th October, the condition of the organs and numbers of parasites remaining the same.

Case 33.—Bagu Sing, m., 30, out-patient, 2 months ill. Says fever begins with sharp rigor every evening at 6 P. M., examined 20th September at 8 A. M. Spleen enlarged to umbilious; liver not enlarged. Looks well and is not anæmic nor emaciated. Peripheral blood; no parasites. Not seen again.

Case 34.—Manu, m., 25, latterly in-patient, two months ill (?). Diagnosed kala-azar in the hospital. It is difficult to ascertain the duration of the illness in this case; but patient says it is only two months, and that a month ago he was driven out of his village (in consequence of his having kala-azar ?). Says that the fever came daily with rigor and was very severe, but that he is now better somewhat. Examined on 6th October at 8 A. M.; temperature 96·2° F. only. Looks thin and starved; fairly anæmic (not very); no œdema now, but says that his feet were swelled a month ago. Spleen occupies a third of the anterior surface of abdomen and reaches nearly to the umbilicus; liver three inches below ribs; both very tender. Peripheral blood, no parasites nor pigment. Splenic blood; numerous spleen-cells. No parasites and not a particle of pigment, black or yellow, obtained in three specimens. Three punctures of the liver failed; two drew nothing and the third drew only blood without parenchymatous tissue, the blood containing no pigment. Temperatures taken for eight days from this date show a subnormal temperature, (Appendix C—Chart 1). Motions examined on two occasions showed only a few trichocephalus eggs, but were constantly loose and were passed three or four times daily (he says). On 11th the liver was again punctured twice. The first drew a little cellular substance without blood; the second much cellular substance with a little

blood. A sprinkling of melanin in the cells; granules all about 2 μ; not recent, and about one mass only in three or four fields, although the cells are very numerous. Many cells contain typical "pigment ocre" (not bright yellow). Unfortunately the second puncture, being made with a new needle, yielded much rust, which rendered the estimation of the amount and reaction of yellow pigment doubtful; but it was certainly present in small quantity if not in large. Patient not examined again.

NOTE.—Absence of the pigments from the specimen from the spleen, and their presence in the liver. The latter organ appears to have been in a very bloodless condition.

Case 35.—Deobar, m., 22, two months ill. A Native Christian belonging to the American Mission. Began to feel feverish and unwell two months ago. Left Nowgong for the Mikir Hills for a week, and two days after return was seized with high fever. Mr. Parker of the Mission informed me that the fever was continuous without rigors and reached 105° F. once. Was treated by quinine, having been given 150 grains before examination by me. Eight days before examination fever disappeared. Examined 15th December at 9 A.M. Very considerable anæmia; not at all emaciated; feet œdematous; face pale and puffed, especially under the eyelids. Spleen very slightly enlarged; liver not enlarged at all. Peripheral blood, no parasites nor pigment. Motion carefully searched; one trichocephalus egg only—no ankylostomum eggs. On 10th September looked much better and less anæmic and œdematous; colour returning to lips and tongue; but spleen had increased for 2 inches below the ribs, and liver was distinctly palpable and tender. Blood, no parasites. No return of fever. On the 5th October Mr. Moore of the Mission informed me that the patient was getting fever, and took the temperature twice daily; the result showed a low constant fever (Appendix C—Chart 2). Examined on 6th October, the spleen was found to be 4 inches and the liver 1 inch below ribs; both tender on pressure. Anæmia improved and œdema nearly disappeared. Blood, no parasites. Two punctures of the spleen were attempted; one drew nothing, the other drew only a rush of blood, containing no spleen-cells nor pigment. Seen on 20th October, the enlargement of the liver had nearly disappeared, while that of the spleen remained.

NOTE.—The examination of the spleen was indeterminate, no cells being obtained. The history, the early appearance of œdema and of the constant low fever (which was not affected by the daily considerable doses of quinine given) should be noted.

Case 36.—Ashman Ali, m., 18, Hospital Assistant, 3 months ill. Has been having severe fever, irregular, recurrent and preceded by rigors. Lived in the Hospital Assistant's house at the village of Mankola when he was attacked. Several other Hospital Assistants had suffered in the same house previously. Examined on 15th September 10 A.M.; temperature 99·0° F. Slight anæmia. Looks rather ill. Spleen slightly enlarged. No enlargement of the liver. Peripheral blood, several æstivo-autumnal amœbulæ, not pigmented, with "tongues." A pigmented leucocyte. No crescents. Not seen again.

NOTE.—Absence of crescents, but presence of a pigmented leucocyte with unpigmented amœbulæ.

Case 37.—Mulai, m., 20, 3 months ill. No history. Examined on 17th September morning; temperature 98·6° F. Considerable anæmia. Spleen to umbilicus; liver not recorded. Blood, no parasites Not seen again.

Case 38.—Gulasi, f., 10, 3 months ill (very doubtful). The child, who comes to hospital without relative, says she has had occasional slight fever for three months, but that a week ago a very severe attack of came on. Relatives had kala-azar some years ago, and father died of it. Examined 17th September, 1 P. M.; temperature 103° F. Spleen several inches below ribs; liver not enlarged, considerable anæmia, but child appears cheerful and fairly well in spite of high fever. Peripheral blood, no parasites. Examined next day at 11 A.M. Rigor well on; temperature 104·5° F. Blood, numerous unpigmented amœbulæ (æstivo-autumnal) with "tongues"; no crescents or pigmented leucocytes. On 19th, a few amœbulæ; no crescents. Quinine was now given regularly and the child appeared quite well on the 19th October, the spleen having decreased notably.

NOTE.—No crescents; absence of liver enlargement. It is possible that the æstivo-autumnal infection was of only one week's duration.

Case 39.—Jhori, m., 16, 3 months ill. Supposed to be kala-azar at the hospital. Says illness began with high fever. Examined 20th September at 8-30 A.M.; temperature 100° F. Much emaciated; considerably anæmic; feet œdematous. Spleen fills half abdominal area; liver a little enlarged. Peripheral blood, no parasites nor pigment. Not seen again.

Case 40.—Grace, f., 6, 3 months ill. Christian child. No history. Examined 12th October, not emaciated nor anæmic. Spleen not enlarged, but liver one inch below ribs and tender, temperature 98·9° F. at 9-30 P.M. Examination of blood not made.

Case 41.—Tukai Mikir, m., 35, 4 months ill. Hospital Assistants think it a case of kala-azar. Says that two persons have died of kala-azar in his house, and that 8 out of 9 families in his village now have the disease. Captain McNaught thinks the case to be one of kala-azar from the history. Patient says that the disease began with fever, which comes on every third day, that he "turned black," and that his feet were swelled. He is now much better. Examined on 23rd September, morning; temperature 97·4° F. Does not look particularly ill, but is somewhat anæmic and emaciated; no œdema. Spleen fills half the abdominal area; but there is no enlargement of the liver. Peripheral blood, no parasites nor pigment. Splenic blood, spleen cells obtained. Black pigment present in very small amount in some of the cells. No yellow pigment found.

NOTE.—No enlargement of liver, absence of parasites, presence of melanin in spleen.

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Case 42.—Duki, m., 30, 4 months ill. Says fever has been coming daily with rigors at noon. Examined 28th September. No symptoms at all observed. Blood, no parasites. Not seen again.

Case 43.—Bhokou, m., 12, 4 months ill. Thought at hospital to be kala-azar. Several people died of kala-azar in his house some years ago. Is well-known at hospital. Was attacked 4 months ago with severe fever, which lasted without intermission for 10 days. The fever then seems to have disappeared (?) for more than 3 months, but came on again with violence six days ago. Enamined 5th October at 9 A.M., temperature 100·8°F. Looks very ill; is much anæmic, but not emaciated ; yellow colour. Spleen extends to within an inch of umbilicus ; liver 2 inches below ribs and tender. Peripheral blood, not a sign of a parasite nor a grain of pigment. Splenic blood ; cells obtained ; black pigment in almost every field, recent and old ; not copious. Numerous parasites, exactly similar to those found in spleen of Case 23 ; some of them have formed a few large spores ; probably æstivo-autumnal tertian (paragraph 21). No small forms present, no crescents. No yellow pigment found. From this date the temperatures were taken as often as possible and showed the "constant low fever," with a morning temperature of 99°—100°, and an evening one reaching 102°F. Seen again on 17 October. Has been taking quinine, which seems to have improved his general appearance while it has not removed the low fever. Spleen as before ; liver increased to 3 inches below ribs ; both organs tender. Very anæmic (? ankylostomes present—stools not examined). Pronounced kala-azar at the hospital. Not seen again.

NOTE.—This would seem to be a typical case of kala-azar of the first to second stage. Parasites and pigment were found in the spleen. No crescents.

Case 44.—Aziz Rahman, m., 10, 4 or 5 months ill. Is well known at the hospital. His mother and sister died from kala-azar some years ago, and his young brother from fever (? kala-azar) four months ago. Says he has had irregular fever for 4 or 5 months with rigors ; it lasts a week or so, goes away for a while, and then recurs. His father is now getting similar fever. Fever began again with violence on 30th September. Examined 3rd October 10 A.M.; temperature 98·0 °F. Looks sick and yellow ; considerably anæmic, but no emaciation or œdema ; conjunctivæ yellow ; tongue good. Spleen to within an inch of umbilicus ; liver one inch below ribs. Peripheral blood not examined. Splenic blood ; numerous cells obtained. Black pigment, small but in profusion, *i. e.*, some in every field. No yellow pigment. Two typical, nearly mature, quotidian æstivo-autumnal parasites with marked definitions and a single large clump of pigment found. No other forms, amœbulæ, or crescents, although much splenic blood was examined. Temperatures taken from this date showed a nearly normal chart rising occasionally, however, to between 99° and 100°F. Quinine given regularly. Seen again on 17th October, considerable improvement was noted in him. Spleen 1 inch only, and liver just palpable. Says no more fever since treatment was commenced. Has a tendency to goitre, from which his mother suffers and his aunts now suffer. Peripheral blood, one pigmented leucocyte only (apparently crescent pigment). No crescents or other parasites present. Not seen again. The case was looked on as one of kala-azar.

NOTE.—I think there may have been a very few crescents in this case (to judge from the pigmented leucocyte), but I could find none on very careful search. There was not extreme enlargement of the organs.

Case 45.—Kolai, m., 8, 5 months ill. Well-known in hospital. Captain McNaught thinks the case is probably kala-azar. No relatives have died of kala-azar, and no one in the house is now getting fever. The boy's father says that the fever was originally very severe, and adds, independently of questioning, that it usually came on every third day only, with rigor, but that for the last two months it comes daily. He declares that the spleen has been enlarged for 2 or 3 months. Examined 16th October, morning ; temperature 99·4° F. Looks ill and is extremely anæmic and considerably emaciated. There is no œdema of the feet, but the abdomen is protuberant in consequence of ascites. Spleen much enlarged (amount not noted), liver 2 inches below ribs ; both organs tender. Splenic blood ; numerous spleen-cells. In two specimens traces of black pigment consisting of very minute granules enclosed in small cells of about 4μ were found here and there—some in six fields or so ; no larger collections or clumps. In the third specimen a mass of parenchymatous tissue was obtained, which contained a vein of copious black pigment consisting of the above small collections, together with larger and blacker clumps arranged in streaks. Yellow pigment in small granules of a bright yellow, angular or rounded, found here and there in the cells, especially in the patch of parenchymatous tissue just mentioned. No distinct parasites found, but some of the pigment clusters look like quartan parasites recently taken up by the spleen-cells. Patient not examined again, but several temperatures taken showed presence of the low fever.

NOTE.—Both pigments in spleen.

Case 46.—Jhuran, f., 4, 9 months ill. Well-known in hospital. Mother died in hospital of kala-azar. Case diagnosed kala-azar. No history ; examined 1st October, morning, temperature 100·4 °F. Fever now rising ; pulsation of carotids ; nothing like rigor, and patient does not look at all distressed. Spleen to pubes and nearly to umbilicus ; liver halfway to umbilicus. Much anæmia, considerable emaciation and some œdema of feet ; ascites. Peripheral blood ; on this and several other occasions, no parasites nor pigment. Morning temperatures above normal.

NOTE.—Presence of low continued fever suggested by the high morning temperatures. No parasites found.

Case 47.—Piruj, m., 3, 10 months ill. Known in hospital and diagnosed kala-azar. Father says he has had fever for 10 months (?), and that it has been continuous for the last

three months. Declares that he has become blacker. Examined 19th September at 3 P. M. temperature 100·2 °F. Considerable anæmia and emaciation; no œdema. Spleen nearly to crest of ilium; liver 2 inches below ribs; abdominal veins slightly enlarged; protuberant abdomen. Blood, no parasites. Temperature taken on several occasions showed constant fever between 99° and 102°F. Blood never showed parasites. Seen on 18th October; has been having quinine in large doses regularly, and his uncle says he is better. Less anæmic and emaciated. Spleen much reduced, but liver larger (3 inches below ribs); both organs tender. Temperature 96·0 °F. (8 A.M.). Splenic blood (two punctures); numerous spleen-cells; no pigment whatever, black or yellow; no parasites.

NOTE.—Low constant fever, apparently improved by quinine.

Case 48.—Makmal, m., 10, 10 months ill. Diagnosed in hospital as kala-azar. Father, mother and a cousin died of kala-azar, the last about a year ago. Says illness began with rigors and very severe fever; the former were very sharp and came every day. Is now feeling better. Examined on 20th September, morning; temperature 98·4 °F. Considerable anæmia and emaciation; does not look particularly ill. Spleen to umbilicus, not tender; liver 2½ inches below ribs, slightly tender. Peripheral blood, no parasites nor pigment. On 21st September at 9 A. M., temperature 96·8. Splenic blood; numerous cells, not a particle of pigment, black or yellow, in three specimens; no parasites. Examined on 16th October at 8 A. M.; temperature 96·2°F. Says he still gets fever (?). Hepatic blood; numerous liver-cells, most of which contain from 5 to 30 angular granules of typical yellow pigment, single or in small clusters. Do not blacken with ammonium sulphide; turn green with Löffler's blue. No melanin nor parasites.

NOTE.—Absence of melanin and parasites from peripheral, splenic and hepatic blood; presence of yellow pigment in large quantity in the last only. Nature of temperature-chart not ascertained.

Case 49.—Dharbari, m., 30, one year ill (?). Says has had slight fever for a year; worse the last twelve days. Examined 3rd October, morning; temperature 97·5° F. Spleen 3 inches; liver just palpable. Does not look at all ill. Blood, no parasites. Not seen again.

Case 50.—Jayob, m., 10, one year ill. Says illness began with fever and rigors; was very severe, but is better now. Examined 28th September morning, considerable anæmia; no emaciation or œdema. Spleen 4 inches, liver 1 inch below ribs; slightly enlarged abdominal veins. Peripheral blood, no parasites. Not seen again.

Case 51.—Bagi, m., 30, one year ill. Says he gets high fever occasionally since one year. Each attack lasts about a week. Acquired the illness outside Nowgong. Examined 9th October, morning; temperature 97·7°F. Has had high fever for several days with rigors. Does not look ill or weak; is yellow but not emaciated and very little anæmic. Spleen to umbilicus, and liver one inch below ribs. Is a gentleman's servant, and is certainly not considered to have kala-azar. Peripheral blood, numerous unpigmented æstivo-autumnal amœbula with "tongues;" many pigmented leucocytes; not a single crescent. Large doses of quinine. Examined next morning; only one pigmented leucocyte was found. On 12th October, says fever has left him since he had the quinine. Splenic blood; melanin in rather large quantity; no parasites; no crescents; no yellow pigment. Not examined again.

NOTE.—Absence of crescents, but presence of pigment with the unpigmented amœbulae "with tongues" —suggesting that the mature stage of this is pigmented.

Case 52.—Shorat Chandrade, m., 25, one year ill. Illness began with high fever without rigors and lasted off and on for 9 months. It has left him (he says) for the last three months. Examined on 19th October at 9 A.M., temperature 98·5 °F. Does not look very ill; no emaciation; some anæmia; feet slightly swelled; abdominal veins a little enlarged, but not much ascites. Spleen past the umbilicus: liver 4 inches below ribs, neither of them tender. Splenic blood, a few spleen cells, no pigment black or yellow; no parasites. Not seen again.

NOTE.—This man was a fairly well-paid official who could afford good food. Hospital Assistants thought it was not a case of kala-azar, because patient was "not ill enough;" they thought it was "ordinary chronic malarial fever." Note also great enlargement of both organs and absence of pigments in specimen from spleen.

Case 53.—Vikhari, m., 52, about one year ill. Is in hospital for some surgical complaint (not noted). Has had slight fever occasionally. An attack for the last three days. Examined on 29th September; not at all ill. Spleen 3 inches below ribs; liver not enlarged. No anæmia. Peripheral blood; no parasites; one pigmented leucocyte. Quinine. No more fever from this date. Slight diarrhœa; motion examined on 8th October; one ankylostomum egg found; swarms of cercomonads in clusters; no amœbæ. Temperature chart showed normal readings.

Case 54.—Harmuz, m., 5, 2 years ill. Well-known in hospital; considered to be kala-azar. Mother said to have died of it. No history. Examined 2nd October, 7-30 A.M., temperature 99·5 F. Enormous enlargement of organs; spleen long past umbilicus; liver 3 inches below ribs (in small child). Abdomen much distended; abdominal veins enlarged. But there is scarcely any anæmia. No œdema, and the child is quite fat and cheerful. In same condition on 18th October. Temperatures taken occasionally have shown morning readings above the normal. Splenic blood; few cells obtained; great rush of blood; no parasites; no pigment, black or yellow.

Nine Kala-Azar In-Patients.

NOTE.—The following nine kala-azar in-patients cases were all in-patients at the Nowgong Civil Hospital, and were all returned as kala-azar, being diagnosed as such by Captain McNaught. Sections of their temperature charts are given in Appendix. C. All were living when I left Nowgong.

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Case 55.—Upar Singh, m., 8, six months ill (?). *Kala-azar.* No reliable history obtained. Examined frequently from 14th to 19th October. Temperatures Appendix C.—Chart 3. Fat and cheerful. No appreciable anæmia; no œdema. Belly protuberant; spleen 2 inches and liver 1 inch below ribs; no enlarged abdominal veins. Peripheral blood frequently examined; no parasites nor pigment. Splenic blood on 19th October; few cells obtained; great rush of blood; no parasites; no pigment whatever, black or yellow. Has been well dieted and treated with cinchona febrifuge for some months. Motions contain no eggs of entozoa nor protozoal parasites.

NOTE.—Slight daily rise of temperature; absence of parasites and pigments.

Case 56.—Bedesi, m., 4, 6 months ill (?) *Kala-azar.* Mother died of Kala-azar two years ago. Has been in hospital since January. No other history. Examined from 14th to 19th October. Section of chart, Appendix C—Chart 4, shows daily rise (which had been going on for a long time previously). Fairly fat; slight anæmia; no œdema of feet; conjunctivæ yellow. Protuberant belly; spleen to umbilicus and ilium; liver 3 inches below ribs; neither tender. Peripheral blood, no parasites on frequent examination. Splenic blood; large masses of pulp obtained; no pigment, black or yellow; no parasites. Motions, a few eggs of richocephalus only.

NOTE.—Daily fever and absence of parasites and pigments from spleen.

Case 57.—Adiram, m., 6, one year ill. *Kala-azar.* Was admitted last July. Mother, a sister and a young brother died from kala-azar 2½ years ago. When asked if he ever felt cold during his illness, the child replies that he used frequently to shiver when it first began. Examined from 27th September to 19th October. Chart 5 shows a low fever. A little emaciated; no œdema of feet (though there was some formerly). Considerably anæmic; conjunctivæ rather yellow. When first examined the spleen extended to umbilicus, and the lower edge of the liver half-way to the same from the ribs; both organs were tender. At the end of the period of examination the spleen had receded by more than an inch and the liver by two inches. The belly was not very prominent, and the abdominal veins not enlarged; no parasites ever found, after several careful examinations, in peripheral blood. Motions contained at first very numerous eggs of ascaris and trichocephalus, also a few eggs of ankylostomes and a thread-worm's egg; no protozoal parasites. After vermifuges (including thymol) a very few trichocephalus and ankylostomum eggs were still found. Splenic blood on 13th October; spleuic cells fairly numerous. Black pigment present in small collections of minute grauules, always inside spleen cells in one out of twelve fields. No parasites or yellow pigment observed. The melanin tends to lie in streaks, and appears to be fairly old deposit.

NOTE.—The presence of melanin proves at least that a parasitic invasion of the blood has lately taken place.

Case 58.—Kali, f., 10, one year ill (?) *Kala-azar.* Her parents, two brothers and three sisters all died of kala-azar some years ago. Examined from 28th September to 20th October; chart 6; temperature shows an occasioual tendency to rise above normal, but is frequently subnormal. Diarrhœa; about 4 motions daily. Stools contained numerous ascaris eggs and a considerable number of ankylostomum eggs, which were not entirely got rid of by vermifuges. Considerable anæmia; marked emaciation; no œdema; abdomen slightly protuberant and abdominal veins slightly enlarged. Tongue fairly red; conjunctivæ slightly yellow. Much pulsation of carotids, but no cardiac bruit, even anæmic. Spleen 3 inches and liver 2½ inches below ribs; neither tender. Patient says both are decreasing rapidly. Admitted 22nd September. Hepatic blood on 23rd nil. Splenic blood on 14th October; numerous cells obtained. A few found to be unmistakably pigmented with melanin after long search, melaniu very scarce. One cell found containing typical yellow pigment; no more seen. Patient improved while under examination. No parasites ever found in peripheral blood after frequent examination.

NOTE.—Diarrhœa, ankylostomes and decrease of organs (?) Also pigments, and their small quantity.

Case 59.—Aiti, f., 8, one year ill. *Kala-azar.* Parents died from kala-azar three years ago; and two brothers and three sisters about a year and a half ago. She herself has been ill for about a year, and has been in hospital since July. The child is old and intelligent enough to answer questions. She repeats that the illness began with daily attacks of cold and shivering and with great heat. Examined from 26th September to 19th October. Not at all emaciated; slight anæmia; protuberant abdomen; enlarged abdomiual veins; no œdema of face or feet; pulsation of carotids. Liver 2 inches below ribs and spleen to umbilicus; neither tender. Spleen decreased by more than an inch during the period of observation. Tongue red; heart, no bruit. Chart 7 shows daily fever between normal and about 101·2° F. Finger-blood frequently examined, no parasites nor pigment. Splenic blood; cells obtained, but not numerous; no pigment, black or yellow. Motions, numerous ascaris eggs, a few trichocephalus and a very few ankylostomum eggs. No amœbæ nor cercomonads. Quinine and cinchona regularly since admission, no marked influence on chart.

Case 60.—Bedu, f., 8, one year ill. *Kala-azar.* Parents and one brother died from kala-azar two or three years ago. Examined from 6th to 19th October. Is quite fat and cheerful; slightly anæmic, has been in hospital for some time. Spleen 2 inches and liver 3 inches below ribs, both slightly tender. Enlarged abdominal views and and protuberant

abdomen. No œdema. Pulsation of carotids, but no cardiac bruit. Blood frequently examined, no parasites nor pigment. Splenic and hepatic blood not examined. Motions, a few eggs of ascaris only. Temperature subnormal—Chart 8.

Case 61.—Pual, m., 8, one year ill. *Kala-azar.* A very intelligent boy, well known in hospital. Seven relatives died from kala-azar recently. Repeatedly questioned, says his illness began with daily attacks of shivering followed by high fever. Spleen become enlarged after he had had fever for some time. Examined from 15th September to 19th October; greatly emaciated, very anæmic, no œdema, cheerful and energetic, enormous enlargement of organs; spleen to ilium, liver three or four inches below ribs; both very tender. Extreme pulsation of carotids with loud aortic bruit. Enlarged abdominal veins. Constant fever—Chart 9; the morning rise of temperature beginning at about 9 A.M., often with a slight feeling of chilliness. Quinine frequently given has had absolutely no effect. Motions 3 or 4 daily, contain numerous eggs of ankylostomes and trichocephalus; the former only diminished in number by thymol. Finger-blood very frequently and methodically examined; no parasites, nor pigment. Splenic blood frequently obtained; pours out of needle, showing great congestion; no parasites nor black nor yellow pigment ever found. Hepatic blood (once) pours from needle, several cells containing typical yellow pigment; no melanin. Case remained unchanged during the month of observation.

NOTE.—A typical case of kala-azar. Complete absence of parasites and melanin.

Case 62.—Daneesh, m., 15, 15 months ill. *Kala-azar.* An intelligent lad, says fever began after the great earthquake in June 1897 and lasted a month, during which there were frequent attacks of shivering. Then an "internal fever" set in, during which his spleen enlarged. This condition has continued to the present. He says his parents and a brother and sister died from kala-azar before and during his illness. They all had fever and enlarged spleens. Has taken much quinine, which he thinks does him good. Examined from 18th September to 19th October. Moderate anæmia and emaciation. No œdema now, but feet were swelled formerly. Pulsation of carotids; no bruit, enlarged abdominal veins, but belly not protuberant. Liver halfway to umbilicus, but spleen only 5 inches below ribs; both tender. Conjunctivæ rather yellow. Daily fever—Chart 10. The amplitude is rather large, and there is a fall below normal sometimes before the daily exacerbation. This begins at about 3 P.M., often with a slight feeling of chill. Quinine frequently given has produced no effect whatever. Finger-blood examined very frequently at all hours; spleen pricked twice and liver once; no parasites, melanin, nor even yellow pigment found. Organs congested, motions twice or thrice daily; an occasional ascaris egg, no ankylostomes' eggs ever found on repeated examinations. Improved somewhat during period of study.

NOTE.—Another typical case of kala-azar. The fever is very interesting, being extremely like a quotidian. The daily constancy is, however, too great; quinine was useless, and no parasites were ever found, even after the most careful search. Great enlargement and congestion of liver.

Case 63.—Domila, f., 8, 2 years ill (?). *Kala-azar.* Parents, brother and sister died of kala-azar 2 or 3 years ago. Examined from 27th September to 19th October. Fairly fat, but considerably anæmie. Belly protruberaut, no enlarged veins. Face and eyelids œdematus; feet not swelled, conjunctivæ slightly yellow. Great pulsation of carotids; slight bruit. Liver 3 inches and spleen 4 inches below ribs; both tender; slight daily fever—Chart 11. Quinine did not affect it. Finger-blood frequently examined; no parasites nor pigment. Spleen, once; few cells obtained; no pigments. Motions, three or four daily, diarrhœa; numerous eggs of ankylostomes; also of trichocephalus, no amœbæ, but swarms of cercomonads, on several examinations.

Three Recovered Kala-Azar Cases.

Case 64.—Konoka, m., 8, out-patient, *Recovered Kala-azar.* Is being treated for commencing goitre. Formerly had enormously enlarged liver and spleen, but has recovered during the last six months. Examined 18th October, fat, not anæmic. No enlargement either of liver or spleen, no parasites. Mother has goitre.

Case 65.—Mahomed Safi, m., 15, out-patient. *Recovered Kala-azar.* Was taken ill three years ago with kala-azar; relatives had the disease. Nearly died a year ago with great enlargement of organs and other symptoms, as certified by Hospital Assistants who attended him. Recovered completely, but has had a *little* fever lately. Examined from 15th September, very slightly anæmic; otherwise appears well. Spleen slightly enlarged and hard. Finger-blood contains a few *crescents*. Spleen blood, copious melanin and one crescent found. Recovery; crescents disappeared early. No enlargement of liver.

NOTE.—This attack of fever is probably quite unconnected with the previous kala-azar. Slightness of symptoms connected with the present parasitic invasion is remarkable.

Case 66—Sri Jut Gunahash Gosswami, m., 29. *Recovered Kala-azar.* See Appendix A, 1; not clinically examined.

Nine Autopsies.

NOTE.—In the following autopsies interest was confined almost entirely to the two pigments and the parasites of the intestine, as immediately required for the purpose of this report. For the pigments, pieces of the organs taken here and there were crushed in the fresh state and examined, while cubes were cut for sectioning afterwards. I have thought it best to hand over the latter work to Dr. Daniels, Colonial Medical Service, now attached to the Malaria Commission, and sent by the Colonial Office to work with me in Calcutta. His large experience in such pathalogy gives his opinion great weight, while his independent testimony in the matter is valuable.

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Case 67.—Gonhor Ali, m., about 30, medico-legal. An overseer of a tea-estate murdered by a cooly; no history; strong and robust man, spleen and liver very slightly enlarged, but loaded with melanin—much more so than in any of the succeeding cases. No yellow pigment found.

Case 68.—Behari Munia, m., 35, three months ill. Diagnosed diarrhœa and anæmia of coolies in the hospital. Admitted on 10th October. Says he had bad fever three months ago, which has now left him. Considerable emaciation and anæmia, no œdema. Liver and spleen not enlarged, much diarrhœa. Died on 13th October as a result of the diarrhœa. *Autopsy.*—A medium sized man. *Liver,* 33 ounces; congested; section normal but somewhat darkened in colour. *Spleen,* 11 ounces; slightly congested; gritty section; pigmented. *Kidneys,* pigmentation of cortical substance in patches. *Intestines,* no entozoa; inflammatory condition and pigmentation in patches of lower part of ilium; no amœbæ or cercomonads.

Microscopically (Fresh—Ross). Very abundant melanin in spleen, liver, sternum marrow, and in areas of kidneys and intestines; old and recent. No parasites. Traces of yellow pigment in spleen; more in kidneys, sternum, marrow and coats of ilium; copious in liver. (Sections—Daniels). "*Spleen,* abundant black pigment, partly in coarse irregular masses not contained in cells, and partly finely-divided and intracellular. No yellow pigment was found, but unless in quantity would be difficult to detect in the midst of the black. There was little fading black pigment. No iron reaction. *Liver,* much yellow, intracellular pigment most abundant at the peripheries of the lobules. Some masses of black pigment in the spaces between the lobules, not intracellular. No iron reaction. *Kidney,* yellow, intracellular pigment in many of the straight tubules. No iron reaction."

Note.—The patient had been given one 3-grain dose of santonin on the 10th October.

Case 69.—Joga Chunar, m., 23, three months ill. *Kala-azar.* Was never seen by me, but history and portions of organs were sent to me by Captain McNaught. Admitted on 21st September; said he had been having fever for about a month before admission. Emaciated; fever; liver and spleen enlarged. Temperature "varied from time to time, but never rose above 102 F." Was finally attacked with dysentery and died on 19th November. *Autopsy.*—Liver 41 ounces; "rather soft, greyish-yellow in colour, pigmented." *Spleen,* 31 ounces, pigmented. *Kidneys,* pigmented. *Intestine,* 7 ankylostomes and 3 round-worms. Large intestines, dysenteric ulceration.

Microscopically. (Sections—Daniels.)—"*Spleen,* much old and some more recent black pigmentation. Slight iron reaction. *Liver,* some black, old interlobular pigmentation. A considerable amount of yellow intracellular pigment in the cells at the peripheries of the lobules. A slight iron reaction. There was some increase of the interlobular fibrous tissue. *Kidneys* contained a small amount of yellow intracellular pigment."

Case 70.—Rogu Tanti, m., 12, 4 months ill. *Kala-azar.* Admitted on 3rd September; said he has had fever for four months. Emaciated; liver and spleen considerably enlarged. No dropsy. Hospital record states that there was no fever after admission. Dysentery set in, organs decreased in size, and patient died on 25th September. *Autopsy.*—*Liver,* 46 ounces, congested. *Spleen,* 16 ounces, congested. *Intestines,* 14 ankylostomes, some 4 feet from ileo-cœcal valve; one trichocephalus; commencing dysenteric process.

Microscopically. (Fresh—Ross).—*Spleen,* a few doubtful specks of melanin; yellow pigment not recorded. Liver, no melanin; a small quantity of yellow pigment. (Sections—Daniels). "*Spleen,* a little black pigment, not intracellular, round some of the malpighian bodies. Masses of yellow pigment in streaks in the stroma. A marked iron reaction was observed in many of the cells—diffuse; in others, showed granules. It had no relation to either the yellow or black pigment. *Liver,* numerous granules of yellow pigment in the hepatic cells, especially in those at the peripheries of the lobules. There was a marked iron reaction, diffuse in some cells, but more commonly affecting only granules. In some cases granules in the cells containing yellow pigment were affected, but more commonly those in other cells showed the reaction; and in many of the lobules the central cells showed the reaction most readily. No black pigment.

Case 71.—Bogi Ratia, m., 24, seven mouths ill. *Kala-azar.* Admitted on 9th September; suffering from fever and enlargement of organs for six months. Emaciated, but dropsical. Liver and spleen enlarged. Occasional fever recorded; diarrhœa; six round-worms expelled after santonin. Died on 17th October. *Autopsy.*—A medium sized man; ascites, dropsy of feet and face. A considerable amount of fat. *Spleen,* 18 ounces, much congested; not softened; section not gritty. *Liver,* 44 ounces; much congested. *Kidneys* congested. *Intestines,* 200 ankylostomes and 8 round-worms; just below the bulk of the ankylostomes, a considerable quantity of bloody mucus full of their eggs; a few whip-worms and a dozen amphistomes in upper part of large intestines. No dysenteric ulceration and no protozoal parasites.

Microscopically. (Fresh—Ross.)—*Spleen;* slight traces of black pigment (?) and a small quantity of yellow pigment in some of the pickings. *Liver,* some questionable granules of melanin; fairly profuse yellow pigment. *Kidneys,* fairly numerous clusters of pale yellow pigment. (Sections-Daniels). "*Spleen;* no pigment, black or yellow, found; no iron reaction. *Liver;* yellow intracellular pigment in fair amount. No black pigment. No iron reaction. *Kidneys.* In patches there was abundant yellow pigment. No iron reaction."

Note.—I agree that the melanin in this case is most doubtful; at the best it was almost indiscoverable.

Case 72.—Hatim Ali, m., 24, ten months ill. *Kala-azar.* Admitted in May for fever and enlargement of liver and spleen; improved; discharged; re-admitted in June for the same with œdema of feet and looseness of bowels. "Fever" is frequently recorded in the hospital history

of the case. Much diarrhœa set in later, and the organs decreased in size. Died 2nd October; *autopsy*, medium sized man, ascites and œdema of feet. Some fat. *Liver*, 46 ounces; congested. Spleen, 40 ounces; congested; not softened; granular section. *Kidneys*, rather congested. *Intestines*, 500 ankylostomes; 2 round and 20 whip worms; very numerous and large amœbæ. Below the ankylostomes a considerable quantity of bloody mucus mixed with their eggs. Dysenteric ulcers of lower bowel containing amœbæ at the surface between the healthy and necrotic tissues.

Microscopically.—[Fresh-Ross]. *Spleen*, no melanin; a small amount of yellow pigment. *Liver*, no melanin; much yellow pigment. *Kidneys*; no melanin; a small quantity of yellow pigment. [Sections-Daniels]. "*Spleen*, granular yellow pigment in patches. No black pigment. Iron reaction fairly marked, mainly affects granules quite distinct from the yellow pigment. *Liver*, very abundant yellow intracellular pigment, massed mainly peripherally. No iron reaction. *Kidneys*, unequal, but fairly abundant distribution of yellow pigment. No iron reaction."

Case 73.—Dashomi, f., 30, one year ill. *Kala-Azar*. Admitted in September for fever, enlargement of the spleen and liver and dysentery. Much emaciated; feet œdematous; tongue red. Temperatures, recorded twice daily, show the low fever. Dysentery continued and organs decreased in size. Died on 12th October. *Autopsy*, considerable emaciation and anæmia; œdema of feet and ascites; no fat. *Spleen*, 12 ounces; not congested. Liver, 18 ounces, fatty, cloudy swelling, not congested. *Mesenteric gland*, slightly pigmented. *Intestines*, 20 ankylostomes; 10 young round-worms; a few whip-worms; and 300 flukes (amphistomum hominis) in large intestine; also extensive dysenteric ulceration with swarms of the protozoal parasites down to the bottom of the ulcers.

Microscopically.—[Fresh-Ross]. *Spleen*, black pigment not very copious; no yellow. *Liver*, black and dark-brown pigment in streaks; copious yellow pigment; fatty degeneration. *Mesenteric gland*, black pigment. (Sections-Daniels). "*Spleen* contained some fairly recent black pigment and some masses of older not contained in cells, in fair amount. *Liver*, some small masses of fading black pigment in the interlobular tissues. There was a very small amount of yellow pigment in a few of the hepatic cells. Much fatty degeneration. *Kidney*, a small amount of yellow pigment; fatty degeneration. A *lymphatic gland* contained a considerable amount of fading black pigment. No iron reactions."

Case 74.—Bhod, m., 12, one year ill. *Kala-Azar*. Admitted, 4th October. Says his mother died from kala-azar nine months ago, and that his brother is now suffering from it. He and his brother were turned out of their village after their mother's death. Declares that his illness began with attacks of shivering and fever, which latterly came with intervals of two days. Says he had enlarged spleen previously, but that liver increased in size during this illness (pointing to epigastrium—information volunteered). Considerable anæmia, great emaciation. Ascites and extreme dropsy of feet. No enlargement of spleen; but liver 2½ inches below ribs and very tender. Diarrhœa and dysentery. Very slight fever occasionally; temperature generally subnormal. Finger-blood frequently examined, no parasites. Liver twice pricked, but very few cells obtained and those were not pigmented. Eggs of ankylostomes found in stools. Two small doses of thymol. Died on 8th November, after my departure; pieces of organs sent to me. *Autopsy.*—*Liver*, 23 ounces; spleen, 5½ ounces. *Intestines*, 102 ankylostomes, 4 whip worms and extensive dysenteric ulceration.

Microscopically.—(Sections—Daniels). "*Spleen*, considerable old, and more recent, black pigment. *Liver*, granules of yellow pigment, but in some of the cells there were rounded yellow masses, in appearance resembling oil globules, but persistent in Canada balsam. Some fatty degeneration. No black pigment. No iron reactions."

NOTE.—Absence of yellow pigment.

Case 75.—Methu, m., 14, one year ill. *Kala-Azar*. Admitted in July with continued fever and great enlargement of liver and spleen; discharged; re-admitted, worse, in September. Some emaciation. Scarcely any anæmia; no dropsy. Spleen nearly to umbilicus with a rounded, painful protuberance in front. *Liver* 2½ inches below ribs, tender. No marked anæmia. Temperature showed daily low fever—Chart 12. Blood from finger frequently examined—negative at first. Spleen and liver pricked once each—no parasites nor pigment. On the 22nd September high fever set in, and patient became comatose on the 26th. On that date, after a most laborious search, I succeeded in finding two small unpigmented amœbulæ, probably of the æstivo-autumnal parasite; but there were no pigmented leucocytes. The spleen had become extremely tender. Motions, frequently examined, showed one whip-worm egg, and no eggs of ankylostomes; but numerous protozoal parasites. Died, comatose, on 28th September. *Autopsy*, shortly after death.—No ascites. *Spleen*, 46 ounces, extremely congested, but no evidence of inflammatory action; no pus or destruction of tissue. *Liver*, 60 ounces; pale; cloudy swelling; not congested. *Kidneys*, pale and yellow. *Intestines*, 4 whip-worms; no ankylostomes, no dysenteric process.

Microscopically. (Fresh—Ross).—*Spleen*, one unpigmented, active amœbula found; no other parasites. I could not satisfy myself that there was any black pigment at all. No yellow pigment. *Liver*, a fair amount of yellow pigment; no black pigment seen by me. *Kidneys*, traces of yellow pigment; not black. *Sternum marrow*, no pigment. *Brain* not examined. (Sections—Daniels). "*Spleen*; much engorged with blood. There was a mere trace of rounded, fine, black, intracellular pigment, such as would be met with in either a recent slight infection or so early that the pigment has barely commenced to be deposited. No iron reaction or yellow pigment. *Liver*; a small amount of yellow intracellular pigment,

most abundant in in the cells at the peripheries of the globules. No black pigment. No reaction with acidified ferrocyanide (iron reaction). No fatty degeneration of the cells, which were coarsely granular. No cirrhosis; but surrounding some of the biliary ducts were numerous cells of newly-formed fibrous tissue. *Kidney;* in one of the sections, a little yellow pigment was found. No iron reaction. The cells were coarsely granular."

NOTE.—It is evident that the final parasitic invasion was an extremely recent one; the organs must have been free from melanin a short time before death. It is, therefore, possible that the invasion was not connected with the previous pathological condition. It is uncertain whether death were due to it, or to the great congestion of the spleen—possibly to both. The brain should have been examined for parasites.

General Observations on the Autopsies.

In all the autopsies the structure of the liver and spleen was quite uniform—there were no necrotic areas, neoplasms, or signs of parasites in the substance of the organs. The capsules were always normal, though perhaps slightly thickened in cases 70 and 75; and there were no adhesions. There was nothing in these organs to suggest any disease but malaria; such as, say, local inflammatory or parasitic diseases. The gall-bladder was always distended with bile. I observed no changes in the suprarenal capsules. In short, except for the absence or paucity of melanin, the picture presented was one which is generally given as typical of paludism. Regarding the minute appearances in the sections, Dr. Daniels says, "In most of the cases there was no marked fatty degeneration of the hepatic or renal cells, in this respect differing widely from the same organs in ankylostomiasis. There was no amyloid degeneration. In the liver, in most cases, there was newly formed fibrous tissue round some of the biliary ducts, but nothing approaching schlerosis, except in case 69. None of the kidneys were cirrhotic or showed any signs of nephritis. The spleen varied more. In none of the cases were the malpighian bodies markedly increased or diminished, but the amount of fibrous tissue in most was in excess. The main interest turns on the pigmentary deposits. Melanin, as the direct product of the plasmodium, is, perhaps, of most importance; it was present in five (out of the eight last cases), but in one (case 75) in such a form as to indicate neither continued nor severe infection. The yellow pigment is evidence and a measure of past hæmolysis, and is only indirectly produced by the malarial organism—being frequently due to other agencies, amongst which I should include as an important one, ankylostomiasis. In that disease, however, deposits in the spleen are very rare, while in this series, when black was not found yellow was, and in the cases in which it was not detected it may have been obscured by the melanin. The iron-bearing cells and granules are also evidence of hæmolysis and no direct proof of malaria. In ankylostomiasis they are occasionally found, but, as a rule, alone in the liver and kidneys; or if, very exceptionally, in the spleen, then in association with the other organs; whilst in this series in each of the three cases in which the iron reaction was met with, it was abundant in the spleen. The appearances in case 74 are not in accord with those in the other cases (as regards yellow pigment). In cellular struction of the organs, the cases without melanin did not differ from those with it."

18. Summary of Cases at Nowgong.—It has been found impossible to arrange these cases in a brief tabular form; but the following summary of the observations will be useful.

Out-patient cases up to one month's duration.

Out of 25 of these (cases 1—29, exclusive of cases 17, 20, 21, 22) *malarial parasites* were found in 19. They were not found in cases 4, 12, 15, 26, 27, and 28. Case 4 had no enlargement of the organs and was probably not malarial at all. In case 27 both black and yellow pigment were obtained from the spleen. Cases 12, 15, 26 and 28 were not examined thoroughly enough to permit me to say that the parasites were actually not present. It is probable then that all these cases, except case 4, were truly malarial. There is a history of *rigors* in 17 of the cases. It is obviously difficult to ascertain the *fever* curve in out-patients, but such observations as were made suggested the ordinary charts. Case 27 had high continued fever for some time, due to the pleuro-pneumonia. Cases 1, 2, 8, 10, 18, 19, 23, and 27 were severe ones; of these, cases 18, 19, 23 were suspected to be kala-azar, and case 27 was actually thought to be so; the first three had quartan infections, the next a tertian infection and the last showed only melanosis of the spleen. This organ was punctured in cases 10, 13, 14, 23 and 27 and contained melanin in all. Yellow pigment was found only in case 27.

The great *enlargement of the organs* is particularly noticeable, even at so early a period. The spleen was enlarged in 16 cases and the liver in 9. A rapid increase during the period of observation was noted in cases 2 (æstivo-autumnal) and 27 (pigments); in case 2 the organs were normal when first examined, but in a fortnight the spleen was 2 inches below the ribs, and the liver

was distinctly palpable; in case 27 the spleen increased by 2 inches and the liver by 1 inch in the same period. In case 6 (tertian) enlargement of both organs after only five days illness was noted; in case 8 (æstivo-autumnal) the spleen was $1\frac{1}{2}$ inch and the liver $\frac{1}{2}$ inch below the ribs after only six days' illness. In case 10 (quartan) the measurements were 1 inch for both organs after 10 days' fever. In case 14 (crescents) the spleen was 3 inches below the ribs after 20 days; and in case 18, the spleen was 3 inches and the liver 1 inch after 30 days' sickness. In cases 25 (quartan), 26 (*nil*) and 29 (tertian) the spleen was 2, 4 and 3 inches, respectively, below the ribs. The maximum sizes reached were in cases 23, 24 and 28, in which the organs were already enormous —so much so as to suggest that the cases were of longer duration than they maintained (obstinately) they were. Neither organs was enlarged in 9 cases; 5 of these were of less than one week's duration; 6 of them showed parasites.

Out-patient cases up to two months' duration.

There are 8 of these—namely, cases 17, 20, 21, 30, 31, 32, 33 and 34. Case 35 is not included, as he was examined into the third month. Of these, *parasites* were present in cases 17, 20, 31, and 32. In case 34 the liver contained both black and yellow pigment. Case 21 was nearly recovered when examined and cases 30 and 33 were not examined sufficiently. Case 17 is interesting: no melanin was obtained from the spleen after recovery four weeks after æstivo-autumnal parasites had been found; and during the same period the organs decreased rapidly in size (quinine). There was a history of *rigor* in all the cases. Typical malarial fever existed in cases 17, 20, 31 and 32; but in case 34 (diarrhœa) the curve was subnormal. Case 34 (pigments) was diagnosed as kala-azar. Enlargement of the *spleen* was present in all and of the *liver* in 6; and was most marked in cases 21, 33 and 34. Tenderness in one or both the organs was complained of in cases 17, 20, 31, 32 and 34.

Out-patient cases up to three months' duration.

Out of 6 of these (cases 35—40), æstivo-autumnal *parasites* were found in cases 36 and 38 only; the others were not thoroughly searched. *Rigors* were recorded in these two cases; were absent in case 35, and are not referred to in the rest. The spleen was enlarged in 5 and the liver in 3. Case 35 is interesting as showing a constant low fever with a progressive enlargement of the organs, but an absence of parasites from the finger-blood—an attempt to examine the splenic blood failed. Case 39 (*nil*) was supposed to be kala-azar.

Out-patient cases up to four months' duration.

There were 3 of these—cases 41, 42, 43. Case 41 was thought to be kala-azar; had a greatly enlarged spleen but normal liver; no parasites, but a small amount of melanin in spleen. Case 42 appeared to have no illness at all. Case 43, supposed to be kala-azar, had great enlargement and tenderness of both organs, with melanin and æstivo-autumnal parasites in the spleen.

Out-patient cases up to two years' duration.

The next 11 cases (44 to 54), and case 22, may be conveniently studied together. Their duration is from 4 months to 2 years; that is, they belong to the period when kala-azar can be definitely diagnosed clinically, and are, therefore, particularly interesting. Six of them—cases 44, 45, 46, 47, 48 and 54, were returned as kala-azar at the hospital; the remaining five being supposed to be ordinary malarial fever. All had one or the other of the organs enlarged and were clinically similar, the kala-azar cases differing from the others only in being graver. Of these, parasites (æstivo-autumnal) were found only in the first and most recent, and melanin with yellow pigment in the second (case 45) only. Yellow pigment alone was found in the liver of case 48. Cases 46, 47 and 54 showed neither parasites nor pigments; but in the first of these, blood from the organs could not be examined. In 3 of the cases (44, 45, and 48) there was a history of *rigors*. In case 44 there were slight occasional rises of temperature; in case 48 there was no record; in the rest there was *low fever* or an indication of it. Both spleen and liver were very large in all six and were enormous in the last (54).

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Of the five cases returned as ordinary fever (49-53), all were of about one year's duration. Parasites (æstivo-autumnal) were found in one (51) and melanin alone in one (53). In cases 49 and 50 the peripheral blood only was examined, showing no parasites; but in case 52 neither parasites nor pigments were observed in the splenic blood, although cells were obtained and both organs were much enlarged. All five cases had enlarged spleens and four had enlarged livers.

Case 22 (doubtful) showed no parasites, and was of one year's duration. Except for the greater gravity of the kala-azar cases, it was impossible to distinguish them from those supposed to be ordinary chronic malaria.

Kala-azar in-patients.

These nine cases (55 to 63) were carefully examined. No parasites were found in any of them after repeated search; but a small amount of melanin was observed in the spleen of two (57 and 58). Yellow pigment also was obtained from the spleen of case 58; and yellow pigment alone from the liver of case 61. The organs were not pricked in one case (60); in the rest (55, 56, 59, 62 and 63), five cases, the splenic blood showed no pigments whatever, while in case 62 the hepatic blood was equally negative.

Both spleen and liver were enlarged in all; greatly so in all except the first.

There were no accessions of typical malarial fever in any of these cases. Low fever existed in six (56, 57, 59, 61, 62, 63). Occasional slight rises of temperature occurred in cases 55 and 58; and the temperature was generally subnormal in one, case 60.

The motions of all the cases were repeatedly examined. The ova of ankylostomes were found in cases 57, 58, 59, 61, and 63, being rare in cases 57 and 59, and numerous in cases 58, 61, and 63. These three last cases were markedly more anæmic than the rest. None were ever observed in cases 55, 56, 60, and 62, although none of these patients appear to have been treated with full doses (if any) of thymol. Round-worms' eggs were seen in five (57, 58, 59, 60, 62), and whip-worms' eggs in five (56, 57, 59, 61, 63).

Recovered kala-azar cases.

Two of these cases had no enlargement of the organs left; the third had slight induration of the spleen. This case also suffered from a slight, probably accidental, malarial infection (æstivo-autumnal).

Autopsies.

The first two of these (67 and 68) were not returned as kala-azar; both had copious black pigmentation of the organs.

The remaining seven were cases of kala-azar (69-75). Case 69 (three months' duration) showed much melanin; case 70 (four months'), a little; and cases 73 and 74 (one year), a moderate amount. Case 75 (one year) contained the merest trace, due to a very recent invasion, before which he must have been free from it. Cases 71 (seven months') and 72 (ten months') contained no melanin at all.

Parasites (a very few) were found only in case 75, just previous to death and just after.

Yellow pigment was found in all the cases except 67 and 74, being present in case 68, diagnosed "diarrhœa and anæmia of coolies" (no ankylostomes), as in the kala-azar cases.

Entozoa are not recorded in the first autopsy, a medico-legal case (67). None were present in the next one (68), "anæmia of coolies." Of the seven kala-azar autopsies, ankylostomes were present in all except one (75). They were few in three cases, namely seven in case 69, 14 in case 70, and 20 in case 73; but there were 102 in case 74, 200 in case 71 and 500 in case 72. Round-worms were present in cases 69, 72 and 73; whip-worms in cases 70, 71, 72, 73, 74, 75; amphistomes in cases 71 and 73; and dysenteric ulceration in cases 70, 72, 73, and 74. The two cases with the largest number of ankylostomes (71 and 72) were also those in which no melanin was found; but the case with no ankylostomes (75) had also the least black pigment. Again, the

cases with most ankylostomes had also the most yellow pigment; but the one with the next largest number (102) of ankylostomes, case 74, was the only one without any yellow pigment. The cases with iron reaction, 69, 70 and 72, were of rather early duration.

General Summary.

The 75 cases may be divided into two groups at the four months' limit. There were 42 cases of less than four months' duration; malarial parasites were found in 26 (62 %) of these, while melanin alone was found in three more. There were 33 cases of more than four months' duration; parasites were found in only four (12 %), and melanin alone in ten more. Hence, putting the parasites and melanin together (the latter being as clear evidence of malaria as the former), we find that either one or the other was detected in 69 % of the cases of less than four month's duration; and in 42 % of those of more than four months' duration. It is evident that, taking all the cases together, there was an increasing difficulty in finding the parasites as the cases advanced in duration.

Out of the total 75 cases, parasites were found in 30, or 40 %; melanin alone in 13, or 17.3 %; and either parasites or melanin in 43, or 57 %.

Six of the cases were considered to be *possibly* kala-azar. These were 18, 19, 20, and 22, all of the same family, of which the first three contained quartan parasites; also 23, which contained both mild tertian and æstivo-autumnal parasites; and 27, which contained both black and yellow pigments.

Twenty-six of the cases were definitely diagnosed as kala-azar—exclusive of the three recovered cases. They were cases 34, 39, 41, 43-48, 54-63 and 69-75. Parasites were found only in three, namely 43 (æstivo-autumnal quotidian), 44 (æstivo-autumnal tertian), and 75 (æstivo-autumnal). But in the last the parasitic invasion appears to have been an epiphenomenon. Melanin was detected in nine more, namely 34, 41, 45, 57, 58, 69, 70, 73, and 74. Yellow pigment was found in eleven, namely, 34, 45, 48, 58, 61, 69-73, and 75; occurring alone by itself in 48, 61, 71, and 72. Nothing whatever was found in ten of the cases, namely 39, 46, 47, 54, 55, 56, 59, 60, 62 and 63; but in cases 39, 46, and 60, the blood from the organs was not examined; while in none were autopsies performed. In all the seven autopsies on kala-azar cases either black or yellow pigment was observed.

The cases of kala-azar in which no melanin was detected after what I consider pretty thorough examination, were cases 47, and 56 (spleen only examined); 48, 61 and 62 (both spleen and liver examined); and 71 and 72 (autopsies). To these should be added case 75 (autopsy), in which the melanin belonged to a recent parasitic invasion possibly unconnected with the previous morbid condition. Hence we may, I think, conclude that eight out of the 26 kala-azar cases contained no melanin, or melanin in such small quantities as to be inappreciable

Thus, inclusive of case 75, parasites or melanin were found in twelve of the 26 kala-azar cases, or in 46 %. Neither were found after pretty careful search in seven, or 27 %. Of the remainder, 27 %, parasites were found in none, but melanin was not exhaustively searched for.

Out of the nine kala-azar in-patients, the eggs of ankylostomes were detected in cases 57, 58, 59, 61, 63; and out of the seven kala-azar autopsies, ankylostomes were found in all but case 75. Thus, the worms were present in 11 out of 16 cases, or 69 %.

19. Summary of Observations at Naxalbari.—I have already mentioned (paragraph 9) that I examined 34 cases of sickness at Naxalbari in the Darjeeling Terai. Of these 14 were said to be cases of kala-jwar. I could distinguish no marked clinical difference between the kala-jwar cases and 18 of the rest, which were said to be ordinary fever. The blood of all alike was examined; generally only once, as the patients came to me mostly from a distance; but sometimes on two or three occasions.

It is unnecessary to give the cases in detail. They were of varying periods of duration from three days to two years. Parasites were found only in five, or 15 per cent. of them, and only in recent cases. The forms observed were as follows. Two æstivo-autumnal cases, without crescents, one of three days, and the other of six weeks' duration; two cases of mild tertian of one or two months'

duration, the pigment in the parasites being very fine and brown; one case of quartan, of three months' duration.

These cases were practically the most recent ones examined; only one of them (a tertian case) had a spleen enlarged more than an inch or so below the ribs.

In the older cases the organs were more enlarged, and no parasites were observed.

No crescents at all were seen; which is just the opposite of Brown's experience with kala-dukh.

The hepatic and splenic bloods were not examined.

The motions were studied when procurable, and ova of round-worms, whip-worms and ankylostomes found, as usual, in a certain percentage.

The cases were similar in every respect to those examined at Nowgong, except, perhaps, that the liver was not so much affected. They were also similar to a few cases of kala-azar shown to me by Dr. Lavertine and Dr. Price near Nowgong.

20. Summary of my Observations of Paludism in Various Parts of India.—I have studied the parasites of malaria during the last four years in many parts of this country; especially Secunderabad, Bangalore, the Sigur Ghât near Ootacamund, Kherwara in Rajputana, the Darjeeling Terai, and Nowgong—also a few cases at Bombay, Poona, Madras and Calcutta.

I have generally experienced the greatest ease in detecting them in one or two examinations in recent cases in which recovery has not taken place; as, however, the cases advance in duration, especially when the organs have enlarged considerably, there is an increasing difficulty in finding them.

I studied many hundreds of attacks in my regiment, the 19th Madras Infantry, at Begumpett, Secunderabad, The men came to hospital directly they were taken ill, and the parasites were generally detected in the first few fields. It was remarkable that, though the men suffered very frequently from such attacks, there were only two or three cases of enlarged spleen in the whole regiment, which was examined by me expressly for the purpose. In one of these cases these was a daily rise of temperature continuing for weeks; it was not checked even by large doses of quinine, and parasites were never found in the blood; in short, it was exactly like the low fever observed at Nowgong. As it was the first case of such a fever studied by me, I was particularly struck by it.

In Bangalore, from 1895 to 1897, I saw several similar cases and called them "spleen fever." Numerous cases of the kind were observed in the Sigur Ghât and the Darjeeling Terai.

The species of parasites found by me in India accord almost exactly in morphological details with those described by the Italians. They were:—

(1) The so-called *æstivo-autumnal* parasites, distinguished by the appearance of only the younger forms in the peripheral blood during the first days of the illness, and, later, by the formation of crescents in a large percentage of cases. I think that there are at least two varieties of this parasite, one with a tertian and one with a quotidian period. In some localities crescents appear to be formed more constantly and in greater numbers than in other localities (see paragraph 31, note). I have paid very close attention to these forms in connection with the mosquito theory, and may add definitely that they are often not to be found at all in the older cases after a second or third exacerbation—though I have seen them suddenly appear again after a long interval.

(2) The *mild tertian* parasites, characterised roughly by a very active amœba found only in the larger corpuscles as a rule, and by the flagellate forms springing, not from crescents, but directly from spherical elements. I think there are at least *two species* in India—one characterised by an excessively fine brown pigment, the other by a fine black pigment.

(3) The *quartan* parasite, characterised by a sluggish amœba, occupying a normal or perhaps small corpuscle and containing coarse black pigment, and flagellate bodies like those of mild tertian.

I am inclined to think that these diverse forms constitute not only quite different species but different genera—each genus including different species which vary in their effects on the human host, and which possibly require different species of insect for their definitive hosts. This, however, is of course a mere hypothesis—see paragraph 31.

It appears to be inadvisable to attempt any scientific nomenclature for these parasites until their development in the definitive hosts has been accurately studied ; hence, I employ the names now in general use.

As regards my observations of the clinical features of cases of enlarged liver and spleen in various parts of India, I must say without hesitation that cases exactly similar to the worst ones of kala-azar at Nowgong have been observed by me during the whole of my service in India and Burma. In other words, isolated cases of a disease clinically indistinguishable from kala-azar appear to exist throughout the country ; and in some localities, such as the Sigur Ghât and the Darjeeling Terai, are to be found in large numbers.

Some observations of mine on the parasites of malaria in India have already been published [18, 23].

21. The Parasites found at Nowgong.—The only peculiarities worthy of note were the following.—

In the *æstivo-autumnal* parasites, I frequently observed that small amœbæ when quiescent exhibited one long pseudopodium which remained projecting when the other pseudopodia had been withdrawn—the amœbulæ with "tongues." This recalls the observations of Marchoux in the paludism of Senegal [22]. Crescents were very scanty and frequently failed to follow the invasion by the fever-producing forms (possible owing to quinine). As a matter of fact, they were seen only in three cases and then in very small numbers.

The *tertian* parasites always had very fine, brown pigment.

The *quartan* parasites were often contained in small, dark-green corpuscles, recalling the "old-gold" corpuscles. In one case (10) many more sporulating forms were observed in the spleen than in the peripheral blood—which is unusual in quartan. Some of the quartan cases were very severe and showed great enlargement of the organs.

In three æstivo-autumnal cases (17, 23 and 43), I observed in blood from the spleen what appeared at first sight to be simple red corpuscles containing each one or two large rounded grains of typical melanin. On close observation, however, it was seen that these corpuscles showed very active amœboid contractions, especially round the periphery, with a continually changing internal cloudiness. Unfortunately, these forms were so rare that I failed in staining them ; but I concluded that the corpuscles contained parasites with a very indefinite outline. They were very like Marchiafava and Bignami's drawings of the mature tertian æstivo-autumnal parasites [24] ; but the body of the parasite was still less distinct. Case 23 contained also some mild tertian parasites and an impigmented amœbula of the æstivo-autumnal variety. Case 43 contained, as well as these peculiar forms, some large sporulating elements recalling those of æstivo-autumnal tertian. Case 23 had great enlargement of the organs and came from a kala-azar stricken village. Case 43 was definitely pronounced at the hospital to be kala-azar.

These forms, and the quartan parasites in dark-green corpuscles, were the only elements which I do not remember to have seen elsewhere, and which have not been previously described (so far as I know).

As mentioned in paragraph 18, parasites were found in only three out of the 26 kala-azar cases, and were all æstivo-autumnal ; but quartan parasites were found in three of the suspected cases, and æstivo-autumnal together with mild tertian in another.

The *intestinal parasites* found at Nowgong were referred to in paragraph 18. They call for no remarks ; save that in two of the autopsies, bloody mucus full of the eggs of ankylostomes was observed in the intestine below the part where the bulk of these parasites were attached.

Objects very similar to those figured by Giles [3] and mentioned by Powell [19] as *coccidia* were frequently observed by me in the dejecta at Nowgong and in the Darjeeling Terai ; and in a case in the latter locality were found in the pus of a cancrum oris of the cheek connected with the mouth. But I could not satisfy myself that the bodies seen by me were not vegetable cells of some kind derived from the food.

IV.—The Pathological Difficulties Discussed.

22. Position of the Argument.—We are now in a better position to discuss the pathogenesis of kala-azar.

It has already been possible in going along to attenuate the issues on this point. In paragraph 11 it was shown that the symptomatology alone, as previously arrived at, sufficed to exclude the ankylostomum duodenale as the pathogenetic agent. On the other hand, the striking similarity of the disease to paludism was pointed out in the next paragraph ; but on closer examination (paragraphs 12, 13, 14) I determined that it would not be safe to trust this similarity alone as sufficient to warrant a conclusion as to the nature of the disease. Indeed, it was shown that there were many possible, and some very forcible, arguments against the malarial theory.

The position of the discussion at that point may be summed up as follows:—

For the malarial theory—

(*a*) The symptoms of kala-azar are almost, if not quite, identical with those of malarial fever.

(*b*) The disease occurs in malarious regions.

(*c*) Most of the cases contain yellow pigment.

Against the malarial theory—

(*a*) The high death-rate of kala-azar.

(*b*) The intractability to quinine.

(*c*) The existence of a low constant fever, not amenable to quinine, and not like malarial fever, in the second stage of the disease.

(*d*) The apparent absence of the parasites and melanin of paludism from many established cases of the disease.

(*e*) The communicability of kala-azar from the sick to the healthy ; and its epidemicity.

It was finally determined, then, that these questions could not be properly discussed without having recourse to further observations ; and the best method of research was judged to be the comparison of a number of cases of fever, including cases of kala-azar at Nowgong. These observations are given in paragraph 17, and are summed up in paragraph 18. We may now ask, what deductions, if any, can be drawn from them ?

23. Deductions from the Observations at Nowgong.—On referring to paragraph 18 it will be seen that out of 75 cases examined at Nowgong, 26 were definitely diagnosed at the Civil Hospital to be cases of kala-azar, 6 were supposed there to be probably so, while most of the remainder were thought to be ordinary fever. The first question is, what difference was observed between the cases of kala-azar and those of ordinary fever ?

Of course, owing to most of the cases being out-patients, many of them were not examined very thoroughly, but at the same time many were examined thoroughly—at least thoroughly enough for the purpose of this report ; while nearly all of them exhibited a striking uniformity of symptoms. In short, it appears to me permissible to extract a definite answer to the question from these observations. And the only answer can be that, if there was any difference at all between the cases of kala-azar and of ordinary fever, it was only a difference of *degree*. The cases diagnosed as kala-azar were, perhaps, more severely ill than those considered to be ordinary fever cases—that was all ; no difference whatsoever in *kind* could be detected.

I think that this must be admitted from a perusal of the cases ; it was certainly very apparent from the actual inspection of the patient.

In other words, to judge from my observations, all the cases examined at Nowgong (excepting perhaps cases 4 and 42) were examples of one and the same disease. On reading the cases from those of the shortest to those of the longest duration and excluding some of the least typical ones, we are almost tempted to imagine that they constitute records of the *same case* taken from its beginning to its end. We have in the earliest cases the sudden onset of fever, generally with rigors, and the early appearance of enlargement of the organs; next an established enlargement of the organs with a low constant fever in the worst cases ; and lastly a cachexia.

If anything serves to establish this similarity and continuity of the cases, it is the gradual evolution of that symptom which is, perhaps, their leading and characteristic feature —I mean the enlargment of the organs. Take the earliest cases—of less duration than a month ; we perceive at once the beginnings of this enlargement, and even a notable increase, after a few days' fever (cases 2, 6, 8, 10, etc.). In case 8 for example, after only six days' illness, the spleen extended to an inch and a half below the ribs, and the liver to half an inch; while in one case (28), who declared he had been ill for only one month, the liver was two inches below the costal arch and the spleen extended to the umbilicus. To leave no doubt as to its very rapid enlargement of the organs at Nowgong, we have cases 2 and 27, in which a marked increase was noted within a fortnight (paragraph 18) during which the patients were observed. Considering next the cases of two, three and more months, we find an ever progressive enlargement in the main, sometimes of one organ sometimes of the other, often of both ; until, finally, we observe the huge tumors of cases 51 and 52 (fever, one year) or of cases 46, 54, 61, 75 (kala-azar), for example. Last of all we have the final diminution of recovery or cachexia (cases 64, 73 74). This symptom is in fact as it were a thread on which all the cases are uniformly strung together. It is the dominant note of nearly all of them, and its gradual development may be watched in them from the beginning to the end.

Considering the *fever*—it is of course evident that complete charts could not often be obtained in out-patients, but such thermometry as could be practiced together with enquiries of the patients, served to elucidate the nature of the curves. In the early cases we have a high fever broken up by periods of complete intermission —in fact, generally of a subnormal temperature, especially in the morning; in the later cases there is a regular chart, a daily fluctuation between proximate limits persisting indefinitely and generally showing a raised morning temperature. And there is evidence of this latter kind of fever, not only in the kala-azar cases, but in case 35 for example, and also in similar cases seen in other parts of India (paragraphs 19 and 20).

All this, however, is practically a mere repetition based on my own observations of the symptomatology of kala-azar given in paragraph 6 and deduced largely from the statements of medical officers transcribed in Appendix A : and we may now turn to the more minute pathology of the cases. Here, again, we observe the same uniformity in all of them, whether they be called ordinary fever or kala-azar. At first, in the early cases, the parasites are found with great facility; later as the disease advances into several months, they are discovered less and less readily, though when not observed in the peripheral blood, they or their immediate product, melanin, can generally be detected in the spleen or liver ; finally, when the enlargement of the organs has become very marked and the low fever is established, we fail to find either the parasites or the melanin at all in most of the cases. And precisely the same law holds both in the cases diagnosed as kala-azar and those supposed to be ordinary fever.

In the early cases we have commencing enlargement of the organs, a broken temperature curve and the presence of parasites.

In more advanced cases we have a more advanced tumefaction of the organs, with increased difficulty in finding the parasites, but, generally, with the presence of melanin in those organs.

Still further, we get the established enlargement of the spleen and liver, the constant low fever, together with an absence of both parasites and melanin. Here, however, we frequently find the yellow pigment.

Lastly, we have the period of recovery or cachexia.

The observations made at Naxalbari, and described in paragraph 19, tend in same direction. Not only were the cases of ordinary malarial fever indistinguishable from those brought to me as instances of kala-jwar, but all alike were almost exactly similar to the cases examined at Nowgong. There was the same enlargement of the organs; the presence of similar parasites in the early cases ; the absence of those parasites and the existence of the low fever at the advanced stages of the disease.

In other parts of India (paragraph 20) I have often noted the absence of parasites and the presence of low fever in old cases of paludism, especially with much enlargement of the organs. In my regiment at Secunderabad, however, when the soldiers were treated early with quinine, I observed very little

enlargement of the organs and scarcely any of the low fever, while the parasites were found with the greatest facility.

Finally, any one who has examined rural fever in India will recognise that the enormous splenic and hepatic tumours of kala-azar are very far from being present only in Assam. I venture to think that cases with similar enlargements are be found almost in every district in this country; more so in some localities, of course, than in others; but still almost everywhere.

But it will now be asked, if the similarity of kala-azar to ordinary fever be so great, how is a diagnosis ever effected at all? Laying aside for future consideration the epidemiological test—that in kala-azar there is a history of relatives of the patient having suffered from the disease, or that he has come from a kala-azar stricken village—and considering the matter only from a pathological standpoint, the answer is that in my experience a diagnosis of kala-azar depended simply on the greater degree of enlargement of the organs and on what was probaby chiefly a consequence of this, the greater illness of the patient as evinced by the greater severity of his low fever, anæmia, emaciation, œdema, and so on. In cases 49, 50 and 53, for example, there was only a medium enlargement of the organs and the patients looked well and cheerful—they were cases of ordinary fever; in cases 51 and 52 there was great enlargement of the organs, but still the patients looked well and cheerful—they were cases of ordinary fever: in cases 44—48, however, the enlargement of the organs was extreme, the illness well marked,—the cases were kala-azar. In other words, the differential diagnosis appears to depend pathologically solely on a question of degree, not of kind.

To sum up then—we arrived very early at the conclusion that the symptoms of kala-azar are strikingly like those of paludism in general. But the observations recorded in the preceding section go further. They exhibit cases of kala-azar and kala-jwar existing side by side in the same localities with numerous cases of paludism and indistinguishable from them, at least by the tests applied, except in regard to the degree of illness present. They establish the presence of the parasites and melanin of paludism in a large percentage of early cases of fever at Nowgong. They show that in many of these early cases in which the parasites existed there was already the beginning of that notable enlargement of the organs which, when further developed, is the characteristic of kala-azar. They prove that the parasites or melanin existed in some early cases which were actually diagnosed as kala-azar. They demonstrate the evolution of the cases from the earliest days of what are quite unquestionably malarial fevers into either cases of ordinary chronic malarial fever or of kala-azar, according only to the degree of illness arrived at. And, finally, they record in many quite established cases of kala-azar the presence of that substance which, while it is not peculiar to paludism, has long been known to be confined to it and a very small group of diseases—the yellow pigment. In short, they convert what was a mere symptomatological analogy into what may appear to be a pathologieal identity.

24. Objections against the Malarial Theory considered.—But the difficulties in the way of accepting this view referred to in paragraph 22 still remain to be discussed—no light task.

Two of them, however, the great fatality of kala-azar and its intractability to quinine, may I think be disposed of easily enough.

In regard to the first we may enquire, (*a*) is ordinary malarial fever never a very fatal disease? and (*b*) are we quite sure that kala-azar is as fatal as supposed? The fact is that malarial fever, is under certain conditions, an extremely fatal disease. We have only to instance the deadly fevers of the African coasts and the Indian terais as examples. It is true that the ordinary malarial fevers met with in most stations in India are far from being fatal. In the cases occurring in my regiment at Secunderabad, for example, several hundreds of which were examined by me, I remember only one or two deaths to have occurred; even without quinine spontaneous recovery was common; and enlargement of the organs rarely took place. Everyone is familiar with fever of this type—it is not serious. But occasionally in most places, and frequently in some, we observe attacks of a more severe nature, either causing death by pernicious access or leading to the long train of secondary symptoms with which we are so familiar. Where such cases abound we have the typical malarious locality, and

in such places a fatal issue results very frequently. It is, therefore, no argument against the malaria nature of kala-azar to say it is a very fatal disease. I do not suppose that the wave of kala-azar now spreading in Assam is more fatal than the endemic fever found continually in many terais in India. We are more struck by the former because it is a new invasion of a tract formerly comparatively healthy; whereas in the terais the fever has existed for years and has in fact rendered them almost uninhabitable. But are we not justified in supposing that, if we could move all the conditions which produce terai fever into the heart of a crowded population—say that of Calcutta for example—a most deadly pestilence would be produced?

Again, the actual percentage of deaths and attacks in kala-azar must be difficult to estimate, for the simple reason that the attacks cannot be identified owing to their similarity to malarial fever. It is not fair to point to a case of enormous tumefaction of the organs which will almost certainly have a fatal termination, and then to adduce it as an example of the great fatality of the disease. This would be to ignore the possible eventuality that many cases recover before ever reaching such a stage. As Price says (Appendix A) "when a case is cured we have our doubts whether it has been kala-azar." At the same time we know that kala-azar is very fatal because of the great mortality caused by it in given villages and hamlets; although here, again, doubts may be expressed in view of imperfections of registration. On the whole, I think we may safely say that there is no reason for supposing that kala-azar is a more fatal disease than paludism at its worst can be.

Similarly with regard to the inefficacy of quinine—we know as a fact that may local fevers, especially those occurring in malarious districts, are singularly resistant to the drug; and before accepting as an absolute fact that it is inefficacious in kala-azar we require to learn many details as to how and when it was given. Quinine should be administered at the proper moment (before the access, generally speaking), and should be given in large enough doses and and be continued for a period long enough to ensure destruction of all the parasites in the system. Again Price's remark in this connection just quoted must be carefully remembered; while, lastly, as I shall suggest in paragraph 41, quinine may be given and may fail in a certain stage of malarial fever without prejudicing the diagnosis. (Compare McNaught, Lavertine, Price and Macnamara in the Appendix with the above remarks). One thing we do know for certain, and that is that numerous cases of paludism all over the world die in spite of a continual exhibition of the drug.

Why paludism should be more fatal and quinine less effectual in some cases and localities than in others does not concern us here (see however paragraph 31); but the fact remains, and I think that the objections to the malarial theory just referred to have little weight.

Those which remain are far more serious. I propose to consider together the presence of the low fever and the absence of parasites and melanin in established cases of kala-azar; and shall then proceed to examine the epidemiological difficulty.

25. The Special Pathological Problem of Kala-azar defined.—In paragraphs 13 and 14 it was pointed out as a result of my first examinations of kala-azar cases, that the really tangible objection to the malarial theory of the disease lay in the absence of parasites and melanin in its later stages, even at a time "when the fever and the general condition of the patients showed that a morbific agency, whatever it is, was most certainly at work." A possible explanation of this apparent anomaly was suggested, but it was noted that the explanation involved a hypothesis which could not possibly be accepted without further observations and without sufficient authority from literature.

The further observations were made. Their result is given in paragraph 23. It cannot be denied that they give very strong evidence indeed in favour of the malarial theory. At the same time, however, they fortified equally the evidence regarding the absence of parasites and melanin in old cases. Further than this, several of the cases, such as cases 21, 35, or 52, tended to show a similar phenomenon in patients who were thought to be suffering from ordinary paludism; while the same thing was suggested by not a few observations of mine in other parts of India, notably the Darjeeling Terai and the Sigur Ghât. Lastly, Gibbon's case of reputed kala-azar transcribed in Appendix B, may be cited as a partial confirmation of my results.

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Similar remarks may be made regarding the low constant fever, which is certainly not malarial in type and which may be thought to be incompatible with a malarial pathogenesis.

How explain the abnormity? If kala-azar be malarial fever a similar state of things should be also found, at least in a certain percentage of cases, in malarial fever generally. What authority in literature have we for supposing such to be the case? And if we find the authority, how explain the fact?

The problem is defined in the following question. *Is it possible that a malarial infection may reach a stage at which there is great enlargement of the organs accompanied by a persistent low fever, but in which neither parasites nor melanin are found even after careful search?*

Accepting as an absolute fact that the beginning of every case of paludism coincides with an invasion of the blood by the pathogenetic parasites, we may disintegrate this question into two simpler ones.

(*a*) *Is it possible that the parasites and melanin may disappear after some months of illness, either definitely or at least for long periods?*

(*b*) *Is it possible that after they have disappeared, great enlargement of the organs, together with a low fever, may remain?*

Let us first examine what existing literature on malaria has to say on the subject.

26. Literature bearing on this Problem.—The literature of paludism embraces three periods. *First*, the early symptomatology and epidemiology culminating in the works of Torti and Pringle in the seventeenth and eighteenth centuries; *secondly*, the pathological anatomy based on the discovery of the black pigment by Meckel and Virchow in 1847 and 1849, and culminating in the work of Kelsch and Kiener in 1889; *thirdly*, the discovery of the parasites by Laveran in 1880 and the subsequent study of them by a host of observers.

The literature of the last period is most voluminous and, on the whole, most careful and exact; but, unfortunately, it has one important deficiency—most of the observations on which it is based were drawn from patients of the European race. It is true that Laveran's own work was carried out in Algeria, and that other studies have been made on patients of less civilised races; but the fact remains that most of the more elaborate monographs have been written in Europe and America. Now, a European takes quinine as a rule, and does not often live permanently in such malarious localities and in such squalid conditions as the native of tropical climates.

Again, this absence of literature on indigenous tropical malaria suggests that there may be varieties of the parasites differing from the known ones—not necessarily morphologically, but in their effects on the human body—which have not been studied at all.

The fact is that the deficiency is a very serious one as regards this discussion. The cases on which my observations were made were nearly all natives of India and lived in the most insanitary conditions, while they certainly very rarely thought of taking quinine, or, if they did so, contented themselves with a dose or two. In such, the first invasion of parasites is probably followed by numerous reinforcements of them from without—the patient is infected over and over again. No steps are taken to check their numbers and they occupy the host indefinitely at their pleasure, until either death takes place or recovery ensues as the result of some systemic re-action against them. The effect may well be an enormous enlargement of the organs, and a final condition of cachexia. Such cases are, of course, seen everywhere amongst malaria-stricken aboriginal populations. With Europeans we have a very different picture. The patient, quite aware of the dangers of malaria, has either hurried away as fast as possible from the malarious spot where he has contracted the disease, or has run to the first medical man for treatment, or has freely cinchonised himself. The force of the infection—probably a single one—is broken, if not subdued, by the medication. In the case of infections occurring in the temperate climates of Europe and America, it is probable that the virulence (or perhaps we should say, numerosity) of the invasion is seldom so great as in hotter countries. The result is that, in place of the frightful cachexias of the poor natives of tropical countries, we find in the European as a rule only very broken and modified examples of

the disease; while the first incidence of the invasion may produce graver effects in the European, it is seldom we see in him the enormous hepatic and splenic enlargements observed in the other. In short, in Europe and America we find mostly the fevers of the early invasion; in India, we observe more the illness of the cachectic.

It would be strange if this state of affairs were not reflected in the writings of European and American observers. In fact, on reading such of their classical works as are based on the theorem of the parasite, we should imagine that a malarial infection consists of little more than periodic attacks of ague, and the incidents attending them. Chronic paludism is dismissed usually in a few paragraphs.

We have, indeed, elaborate pictures of the pathological anatomy; but here, again, the point of interest lies in the changes produced by the early invasion—the distribution of the parasites, their occlusion in cells, and the deposition and elimination of the black pigment, with, perhaps, some excursions into the region of the anæmia and the deposition of the yellow pigment. These are, of course, most important and interesting; but they do not assist us much in our consideration of the present problem. The gradual disappearance of the parasites (and it is evident they must finally disappear in cases of recovery), the ultimate disposal of the melanin, and the slow development of the symptoms and pathological anatomy as the disease progresses towards either of its conclusions are not dealt with in nearly sufficient detail to help us here.

I have, therefore, scarcely succeeded in gleaning many illustrative instances from the later literature on malaria (such as is based on the parasitic theorem) which I have access to; but I may quote a few passages. It is, of course, understood everywhere that the parasites disappear, sometimes spontaneously, in cases of recovery; this fact requires no corroboration. It is more necessary to emphasise the rule that they are found less and less readily as chronic cases advance further—though this also is pretty generally understood. Laveran says in his latest work [25, p. 175] "when the cachectics have not had an attack of fever for some time the examination of the blood does not reveal, usually, the presence of parasites. Amongst those who have returns of fever we find, on the contrary, the characteristic parasitic elements, and often in great number." Further on [p. 275] he remarks of the same class of cases.—"The histological examination reveals the existence of the parasites in the spleen and often in the liver, but in much smaller numbers than in subjects who have died of pernicious access; it can even happen that the parasites have disappeared completely at the moment when the alterations of the liver, spleen, kidneys and lungs have caused death;" and again, "Histological examination of blood taken from the heart or veins does not ordinarily reveal the presence of the parasites which are so numerous in the blood of the individual dead of pernicious attacks." Davidson [26, p. 198] says, "In the advanced stages of the cachexia, parasitic forms may be entirely absent;" and [p. 190] "How far the final cachexia is to be ascribed to the direct action of the parasites, is still doubtful." Thayer remarks [27, p. 192].—"The condition of the blood varies according to the nature of the case. If the cachexia be due to a continued uncured tertian or quartan infection, we may by careful search find an occasional characteristic parasite. Often, though, between febrile attacks it may be impossible, on ordinary examinations, to discover any organisms. If the infection be with the æstivo-autumnal parasite, crescentic and ovoid forms are frequently met with." Manson, however, says [14, p. 23], "A long standing case of recurring malaria with marked cachexia will afford the next best opportunity" (of finding parasites). And, "The pathology of malarial cachexia is virtually that of acute malarial disease." But he makes this important discrimination, "There may be said to be two degrees or kinds of malarial cachexia. In one there is merely anæmia, with congestion of the portal system. In the other there is, in addition to anæmia, organic disease of the abdominal viscera—of the liver, spleen, and kidneys—the outcome of long standing congestion of these organs. These tissue-changes not only keep up the anæmia, in spite of removal from malarial influences, but, in the long run, inevitably progress to a fatal issue."

The reference to the fevers of chronic paludism are most obscure as regards the present discussion. Laveran [p. 175] notes that the attack often

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differs from the classical type, and that "many of the patients do not have rigors and scarcely perceive that they have fever"; and that quinine, even in strong doses, suppresses only some of the attacks. Davidson mentions [p. 186] that the fevers "show a tendency to run on interminably" if untreated; and Thayer remarks [p. 191] "There are often frequently recurring slight febrile attacks, and commonly a regular evening exacerbation of temperature, rising as high as from 100° to 102°. Mannaberg mentions [28, p. 387], that "the Italian investigators, as well as Sacharoff, say that there is a *Febris secondaria post malariam*, a fever which lasts for some days or even weeks after the parasites have ceased to be found, and which does not react to quinine;" but adds that he has not been able to observe it.

These statements, except Mannaberg's, are not express enough to assist us much. It is obvious that as long as attacks of typical malarial pyrexia appear, so long shall we find parasites; and it is evidently to such cases that Manson refers. The difficulty of finding parasites in very advanced cases is also noted; but there is no record touching the question of their gradual disappearance and that of the melanin. As regards fever, while Davidson and Thayer seem to refer to something like the low fever found in many cases, they do not appear to question that it is a parasitic fever. The "Italian investigators," however, have a definite statement to this effect (I regret I cannot obtain the reference).

It may be said here, however, that these quotations appear to suggest that the parasites are found more persistently in the European cases than in mine—which seems to be just opposite to the inference I have attempted to derive from the infection being probably milder in the former than in the latter. The matter is one of great interest, and I shall presently endeavour to to account for it (paragraph 30).

The literature on the parasites in India is contained chiefly in papers by Vandyke Carter [29], Crombie [30, 31], Maynard [32], Rogers [33], Murray [34], Sturmer [35], and myself [18,23]. Those papers are mostly concerned with the parasites themselves, and I can find in them no very apt references to the present matter—except one in the admirable essay of Vandyke Carter, to be quoted presently. Maynard, however, gives a table of 70 cases with very exact details, from which I collect that he found no parasites in advanced cases of paludism. The passage which I refer to in Vandyke Carter's work [p. 163] is headed "Secondary fever," and is so important that it should be quoted *in extenso*. It is as follows.—

"*Secondary fever.*—The spirillar investigation (Work, pp. 171 and 420) led me to recognise pyrexial states following closely on the specific, and similar enough to admit of confusion, which are yet distinct in not presenting the same visible blood infection; and I considered such consecutive, residual or sequelar pyrexia to be the effect of secondary quasi-septic contamination, or possibly of a re-action of the nervous system. Demonstrated so far for the typical spirillar, secondary events of this kind may be usual in other infections; and in the malarial, they appear to be represented by the so-called amphibolic stage of ague, long since noted by Wunderlich and his English commentators. At the native hospitals here, confirmed malarious subjects are seen presenting smart yet not distressing febrile paroxysms, samples of which, in my hands, seemed unattended with pigmented blood organisms, and, therefore, were regarded as of such secondary character; care being, however, needed to distinguish them from negative intercurrent paroxysms in the visibly infected, such as witnessed in Case No. 3. How far the more prolonged fever of equally idiopathic aspect which is often seen in malarious subjects can be viewed as of this secondary or sequelar character remains for the present undecided; the spleen may be moderately involved, but the blood contains no pigment organisms; and quinine has no peculiar efficacy; signs of enteric fever are absent. This class of cases represents one form of the so-called 'malarial remittents,' which amongst natives take the place of 'continued fevers,' so termed in rather antiquated phrase; and, upon review, the data at my disposal indicate that in such cases the absence of visible dotted parasites is not warrant enough to negative an antecedent connection, at least, with genuine malarial infections."

It is known that Vandyke Carter took up the study of the parasites at a very early stage in the history of our knowledge of them, and that there are passages in his essay which justify us in thinking that he overlooked, apparently purposely, the unpigmented amœbulæ of the æstivo-autumnal varieties. Nevertheless, in the "confirmed malarious subjects," to which he seems specially to refer, these varieties should yield the large and grossly pigmented crescents which Carter would certainly never have overlooked; while the other varieties are of course always pigmented. Hence, I think we may admit that he did observe a secondary fever in confirmed malarious subjects in which the parasites were not to be found. I invite attention to every term of this remarkable passage, which is quite worthy of the most distinguished of our Indian observers.

And fortunately, although I have been able to cull few observations pertinent to this discussion from literature based on the parasitic theorem, I can cite some very striking passages from a work of an older school. The work I refer to is perhaps the best exposition of the pathological anatomy of paludism which we possess. Perhaps all the better for my present purpose, it proceeds not on the *point d'appui* of the parasites, but upon that of their immediate derivative the black pigment, and on that of the yellow pigment. The authors, practising in a country, Algeria, where, as in India, the chronic cases of malarial fever are almost as numerous and quite as considerable as the early attacks, give as minute attention to the former as they do to the latter; and every statement of theirs is accepted as bearing the highest authority. I refer to the classical work of Kelsch and Kiener [36].

27. Kelsch and Keiner and Daniels on this Problem.—The authors begin by the following definitions :—

"Le poison palustre est un agent essentiellement destructeur des globules sanguins."

They divide the resulting disease practically into three persiods—the acute, the chronic, and the cachexial.

In studying the acute stage (*intoxication paludéenne aigue*) they begin with a description of the pathological anatomy and histology, and give a long disquisition on the black and yellow pigments respectively. They then describe the clinical symptoms and deal particularly with the various forms and incidents, the simple, bilious, gastric, and hæmoglobinuric fevers, cerebral complications, and so on.

With regard to the second stage (*intoxication paludéenne chronique*) they deal closely with the *hypérémies phlegmasiques*; show the gradual elimination of the black pigment and the permanence of the yellow; and describe the fevers of this stage, particularly a *fièvre symptomatique*.

In the third stage (*cachexia hydroémique et gangrène*, and *cachexia paludéenne chronique*) they exhibit the gradual disappearance of the black pigment and the *surcharge ferrugineuse* of the organs; and conclude with a picture of the final condition of the organs.

They do not finally accept the parasite as the *agent destructeur* because at the time there was still discussion on the point; but show themselves as being favourable to the theorem.

The general picture of the pathological anatomy presented by them is one of the deposition of both pigments in the first stage; and of the gradual disappearance of the black pigment and permanence of the irritating yellow pigment in the later stages. The clinical manifestations of the first state are, then, essentially those produced by the *agent destructeur* itself; those of the later stages are the results due to the yellow pigment, or perhaps, more correctly, to the conditions of the organs produced by it.

In the second stage of the disease they devote a whole sub-heading to a peculiar continued type of fever—the *fièvre symptomatique*—which they consider is not due directly to the pathogenetic agent, but rather to the condition of the organs—the *phlegmasies hépatique et splénique*.

The applicability of this system to the questions now under discussion is obvious.

The three stages of paludism described by the authors coincide with the three stages of kala-azar as defined by me.

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The disappearance of the melanin (and, therefore, by implication, of the parasites) and the permanence of the yellow pigment, compares itself with my observations on kala-azar.

The *fièvre symptomatique* coincides with the low constant fever found by me (and others) in the second stage of the disease.

I should like to quote some whole pages, including exemplary cases, from Kelsch and Kiener's work; there is much that is closely applicable to the present subject. A few leading passages must, however, suffice. With regard to deposition of the pigments they say (p. 634, translated.)

"The formation of the one and of the other pigment continues throughout the course of the malarial infection. But, in the same degree as the affection becomes older, two modifications tend to appear; on the one hand, the formation of the melanæmic pigment becomes inconstant and more and more exceptional without one being able to explain the causes of the cessation of a phenomenon considered specific. Have the parasites ceased to multiply? Have they only ceased to produce pigment?—We can only ask these questions."

"On the other hand, the formation of the ferruginous pigment not only does not cease but seems to be augmented, and acquires, in certain cases, an intensity comparable to that which one observes in certain incurable and progressive anæmias. This process, entirely in obedience to the general laws which we have sought to establish in Book IV, presents, because of its chronicity and of the consequent alterations in the structure and tolerance of the organs, some particulars, which must now be put in evidence"—which the authors proceed to do.

In the above passage the deposition of the black pigment is recorded as going on, though constantly becoming less, throughout the course of an infection; and no limits to the process as regards time are mentioned. The following extract establishes a rough shorter limit (p. 413):—

"We cannot easily assign a limit to the duration of the process of resorption (of melanin). It seems to us little probable that the work requires years —as Arnstein thinks; because it frequently happens that among patients who have succumbed to malarial cachexia, only a few months after the beginning of the infection, we find no vestige of melanosis."

In support of this the authors give autopsies in which the black pigment was not observed—see particularly the conclusion of Ob. II, page 622—occurring in the cachexial period.

I translate the whole paragraph referring to the symptomatic fever (p. 565).

"*Concerning symptomatic fever in chronic malaria.*—Amongst a great number of our patients suffering from the chronic infection, we have noticed certain febrile processes for which we have been led to recognise another cause than the pyrogenetic action of malaria.

There exists a pyrexial condition more or less marked which is prolonged sometimes many days and even many weeks after the serial attacks. It consists sometimes of slight evening exacerbations, without initial chills, and showing little elevation of temperature; more often of a continued febrile movement from 38° to 38·5°C. (100·4° to 102·2°F.) and giving a feebly-broken chart.

This fever shows itself more specially after violent attacks accompanied by icterus or hæmoglobinuria. While it lasts, the liver and spleen are always tumefied and are the seat of a dull and continued pain. It is not accompanied by a marked destruction of red corpuscles, and the examination of the blood, practised from the point of view of the black pigment, is generally negative. The sulphate of quinine is without action; and only alteratives affecting the hypochondriac organs are sometimes efficacious.

The *ensemble* of these characters differentiate this febrile condition from that of malarial fever properly speaking. We think that there is reason to connect them with the hepatic and splenic congestions caused by the latter. Chronic hepatitis, such as we observe outside malarious localities, is ordinarily accompanied by a febrile movement more or less marked, above all in its initial periods. *A fortiori*, we may expect a like effect in the parenchymotous malarial inflammations which implicate all the abdominal viscera and of which the evolution is more rapid than that of ordinary hepatic cirrhosis."

Three charts with which these remarks of the authors are illustrated, are given in Appendix C, Nos. 13, 14, 15.

It should be noted that though the writers did not distinguish the parasites, they employed the detection of pigment during life for diagnosis—which is almost the same thing, especially in the older cases in which crescents exist in the æstivo-autumnal infections.

The authority borne by these citations cannot be questioned; and, on the whole, I am disposed to allow that on the strength of them alone a satisfactory affirmative reply has been obtained to the two questions, (*a*) and (*b*), propounded in paragraph 25. The second quotation from Kelsch and Kiener would seem to establish that in ordinary paludism the melanin (and therefore, of course, the parasites) may not be found in the organs a few months after the beginning of the illness, thus satisfying question (*a*). The passage from Vandyke Carter and the third quotation from Kelsch and Kiener, describing very emphatically a *febris secondaria post malariam*, certainly accord in a remarkable manner, not only with each other, but with my picture of the low fever in advanced kala-azar—thus apparently satisfying question (*b*).

It may, however, be pointed out that while we may admit the secondary fever as not due directly to the parasites, there is yet no express statement in Kelsch and Kiener's work to the effect that this fever can occur *after* the disappearance of melanosis—they and Vandyke Carter merely state that it is not associated with the presence of parasites and the deposition of fresh melanin. It may be further objected that a few quotations of this nature, however authoritative, do not justify us in finally deciding a question of such importance.

How obtain more definite proof? The logical course would be to do so by the exhaustive examination of numerous cases of paludism in many parts of India, and, indeed, of the world. But this would imply many autopsies and months, if not years, of research—an affair quite beyond the conditions of this report.

Fortunately, however, I have been able to obtain just the particular information required from Dr. C. W. Daniels, M.B., Colonial Medical Service.

Dr. Daniels, who has been appointed by the Colonial Office to the Malaria Commission instituted conjointly by that Office and the Royal Society, was sent to Calcutta to study with me, and I have consequently been able to avail myself of his large experience. He has been able to study no less than 2,000 autopsies in tropical countries, in 1,600 of which he has searched microscopically for the pigmentary deposits. He has also studied the parasites of malaria, as well as tropical parasites generally, to a large extent. His knowledge of these subjects, he says, was acquired chiefly in British Guiana, where he was able to see much malaria, partly among Indian coolies; and it will be perceived that his experiences are likely to be of the greatest value touching the present subject.

His statement, in which he is kind enough to reply to certain definite questions of mine, is given in Appendix A, 6. It may be summed up as follows:—

(*a*) He finds malarial parasites much less readily in cases of chronic enlarged spleen than in early cases of malarial fever.

(*b*) He frequently finds an apparently non-malarial fever, not amenable to quinine and not accompanied by parasites, in cases of enlarged spleen.

(*c*) In a very large number of enlarged spleens examined *post mortem*, even of patients who suffered from this fever at the time of their death, he detected no black pigment at all.

These observations apply to members of the East Indian race in British Guiana, and have already been published by Dr. Daniels [37].

They complete my citations on the point at issue.

28.—Points still requiring Explanation.—It must now, I think, be frankly admitted that the condition of enlarged organs with fever but without melanin, observed by me in Nowgong, is not confined to that locality.

The question, however, remains whether this condition is due to malaria at all—whether, indeed, it is not some quite different disease which has been everywhere mistaken for malaria. If there is no melanin in the affected organs, how be certain that their enlargement is caused by the parasites of malaria at all, and not by something else?

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This question is of the greatest importance, not only as regards kala-azar, but as regards malaria in general; and not only in respect to academical theories, but in respect to the actual treatment of cases. It can be finally dealt with only by giving a reasonable theoretical explanation of the phenomenon.

I will now attempt this explanation. It will, I fear, involve some hypothetical matter, but, I trust, may still be of sufficient interest to atone for its prolixity.

What, precisely, have we to consider?

The superficial explanation of the phenomenon—that in the condition referred to the parasitic invasion has died out and the melanin been eliminated, leaving, however, a diseased state of the organs which accounts for the secondary fever—has already been mooted in paragraph 14. It is now necessary to go deeper. We must enquire, what is likely to cause the disappearance of the parasites and melanin? Under what conditions is this disappearance likely to be most speedy? What influence is likely to be exerted in regard to the disappearance by the species of parasite concerned? How explain the low fever and other details?

29.—Gradual Extinction of the Parasitic Invasion.—The dependence of the typical malarial intermittent and remittent fevers on the parasites of the red blood corpuscle has long been recognised as being practically an absolute certainty—so much so, that recent writers do not even take the trouble to discuss it. The movement, sporulation and other cytological characters of those bodies, their close analogy with a whole series of similar intra-corpuscular organisms in some lower animals, and, I may now add, the cultivation of one of these in mosquitoes and its introduction into healthy birds, suffice to establish beyond all doubt their parasitic nature. Their causal relationship to the early febrile and some other incidents of paludism is manifest from the facts that the typical melanin found in the disease is produced in their interior and that the accessions of fever depend upon phases in their life-history.

But paludism does not consist merely of attacks of malarial fever. A typical untreated case—especially as seen in very malarious localities—exhibits a long graduated series of such attacks accompanied by a profound affection of many of the tissues of the body. The disease, properly speaking, bears less affinity to such brief infections as those of measles or small-pox, for instance—with their rapidly-produced individual immunity—than to such prolonged infections as syphilis, tuberculosis, filariasis.

We are quite familiar with cases in which ague, accompanied by detectable parasites, continues to appear from time to time in patients who have removed for years to a non-malarious climate. For example, Major Giles, I.M.S., has told me of a lady who still gets fever occasionally, though she has lived in England for nineteen years after she contracted the disease.

What relationship, exactly, do all the symptoms of such a disease bear to the parasitic invasion which we know must have caused its onset, at all events?

Our first difficulty here lies in the following point. We know that if we examine such a case as just noted, we shall probably find the parasites with ease during the attacks of the typical fever; but in the long intervals between the attacks—when the patient appears almost or quite well—we shall probably find nothing. We know that the parasites must continue to live in the system in some way during all these long intervals—under what form and how? Manson [14, p. 7] suggests a *latent phase* of the parasites; and I have sometimes thought that this phase may be similar to the encysted stage of the parasites found in mosquitoes. Thayer, in discussing the question [27, p. 184], says "the specific organism must exist in some form within the economy during this long period of time. It is hardly conceivable that it should remain in the general circulation, passing through its ordinary cycle of existence, without causing any symptoms whatever;" and he falls back on the supposition of Bignami, that there may be an encapsulated form.

Thayer, however, gives no reason why he finds the continuance of the parasites in the circulation so inconceivable. The point must be closely examined, as it is of first importance in the treatment of paludism.

In my experience of halteridium of pigeons and crows in India, I have always found, out of some twenty birds kept under observation, that the parasites once present never disappear, and even remain roughly in the same

number, continuing to propagate themselves indefinitely and without causing any or much discomfort to the host. I suppose that they are so innocuous that they are, so to speak, permitted to reside permanently in the blood in numbers sufficiently large to be always detectable by the microscope. This is especially the case with pigeons, where the organisms are frequently extremely numerous without, apparently, doing any harm whatever. In crows they are usually much less numerous and, I think, occasion a certain amount of sickness. These facts may be expressed otherwise; a *point of toleration* between the host and the intruders appears to be arrived at, which is higher, permitting the parasites to be more numerous the less virulent they are. But, however this may be, we shall perceive that no theory regarding encapsulated forms is required in this species of hæmocytozoa; the explanation that they propagate themselves indefinitely by ordinary sporulation suffices here to account for their continuance.

With proteosoma of sparrows, larks and crows, I have observed much the same thing; but the parasites are usually far more scarce and they seem to produce much more illness (as Labbé has already remarked). In the warm weather in Calcutta, with a noon temperature of about 85° F., only once out of a large number of birds observed, did I note a disappearance of the parasites—and that was just before death from diarrhœa. While, however, the organism seldom vanished entirely, they often showed considerable fluctuations in number. Thus, the birds infected by the bites of mosquitoes (paragraph 1) had at first such severe infections that "from ten to sixty or even more" parasites could be counted in a single field; but in the few which recovered these numbers ultimately declined to a more reasonable limit, at which the "point of toleration" seemed to be reached. In the cold weather in in Calcutta, however, (noon temperature about 70° F.), Dr. Daniels and Rivenburg and myself have noted a much more rapid recovery in the case of birds which we have infected by the bites of mosquitoes, and, frequently, even an apparently complete disappearance of the invaders.

Hence, in the case of proteosoma we may say that, owing to the greater virulence of the parasite, the point of toleration is lower than in halteridium, and may indeed be so low that the parasites become too few to be easily detected by ordinary microscopic examinations. In the cool weather it may be lower still than in the warm season, perhaps because the vital forces of the host are more braced and vigorous. At any rate, in proteosoma as in halteridium, we have absolutely no justification for calling in any theory of encapsulation; we are justified in holding, until anyone proves the reverse, that the parasites continue to propagate themselves in small numbers, perhaps even in numbers too small for detection, so long as they continue to exist at all.

With human malaria it is obvious that the parasites are much more malign than halteridium and proteosoma appear to be to birds, and, therefore, probably cannot be endured in such large numbers—in other words, the point of toleration must be still lower than even in proteosoma, and must usually be below the *vanishing point*. We know by long experience that when the typical fever is present, we can generally find some of the parasites in the small drop of blood examined, but that when the febrile period has passed and has given place to a long quiescent period they cannot be detected (except when the crescents, which do not cause fever, are present). But this does not imply that the parasites have become extinct or that they have entered an encapsulated phase; we have no justification for thinking so; all we know is that they have become too few to be detected in ordinary specimens and apparently too few to cause any fever.

As a matter of fact, we know that the degree of illness generally depends, *cæteris paribus*, on the number of parasites present—not necessarily *found*. We know that if we find one parasite, say, to fifty corpuscles, we may expect a very severe fever; whereas if we detect only one parasite (say of the quartan species, which does not generally accumulate in the organs) in a whole specimen or two, we may expect scarcely any fever. Hence, we may reasonably infer that if the invaders are still less numerous than this, no appreciable fever at all will be produced.

This is just what is continually observed. If there be fever we find the parasites in one or two specimens; if there be no fever, we do not find them (excepting crescents, of course). In other words, taking a case of quartan for

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example, if the parasites are not numerous enough to be found, they are generally not numerous enough to produce fever.

As a rule, we seldom search more than two well-made specimens for the organisms, and if we detect none in these we record the result as negative. Thus, we may say that if the parasites number less than one in two specimens they are below the *vanishing point.* As just said however, if they number less than this on the average, at least in a case of quartan, they no longer cause fever,—that is, they are also below the *fever point.* Hence, we may agree that the vanishing point and the fever point coincide. The point of toleration is probably some way below the fever point, because we can imagine that the parasites may still be numerous enough to evoke a certain amount of occult trouble in the system although they may not be numerous enough to evoke actual fever.

Some figures will serve to fix those ideas. Suppose that a field of an oil immersion lens suitable for searching for the organisms contains 500 corpuscles; and suppose that a well-made preparation of blood contains 100 such fields. Then two specimens will contain 100,000 red corpuscles. Suppose again that we take the fever point and the vanishing point to lie at one parasite in two specimens; this will give one parasite to 100,000 corpuscles at these points.

Now, the total amount of blood in a man is generally put at about $\frac{1}{13}$ of his body weight; a man of 130 lbs. weight will contain 10 lbs. of blood [38, p. 54.], and 10 lbs. of blood contains about 25 billions of corpuscles [38, p. 4.]. Hence, when standing exactly at the vanishing or fever points, the parasites will still number as many as 250,000,000. That is, if they are at all less numerous than this they will neither produce fever nor be found on ordinary examination. In other words, they may exist in *hundreds of millions* in the system without either causing fever or being readily detectable!

These figures may be commended to the attention of those hasty observers who think that the parasites are absent in a case because they cannot detect them on one or two examinations. Of course, the numbers given above are only illustrative, and I know of no exact determinations on the point; but they are near enough to the truth for my present purpose.

If we must search two specimens to detect one parasite when the parasites number as many as 250,000,000, we must search more to detect one when they are less numerous. Thus, if there be only 25,000,000 parasites, the chances are that we must search 20 specimens (1,000,000 corpuscles) before finding one—a labour of some hours; and 500 specimens must be searched when there are only 1,000,000 parasites, and so on.

Yet it is obvious that a few hundred parasites would suffice to keep alive the infection from day to day in a patient. But the chances against our detecting one, when they exist in such small numbers, are enormous. At the same time, if it requires 250,000,000 parasites to produce even slight fever, it is clear that a few hundred are unlikely to have the least effect on the host.

When the parasites are so few that they produce no appreciable effect, we may conjecture that their number stands at or below the point of toleration. In the case of halteridium the point of toleration is high—is above the vanishing point. In proteosoma it is lower, sometimes above and sometimes below the vanishing point. In human malaria it must be below the vanishing point, because when we can find the parasites (exclusive of crescents) there is almost always fever or illness.

Of course, all this must be admitted to be theory until someone undertakes the necessary laborious studies. But it is a sounder theory than the one of of encapsulation. There are no observations to support the latter; no encapsulated condition is required to explain the facts; and in halteridium we can actually watch the continued propagation of the parasites occurring by means of the ordinary sporulation process. At all events, the first theory gives a wonderfully homogeneous picture of a continued malarial infection. Instead of having to imagine periods of ordinary propagation, alternating with periods of encapsulation, we are called upon to conceive for all kinds of malaria only what we see in halteridium—a continued pervasion of the blood by the parasites multiplying indefinitely in the usual manner.

There is, however, this notable difference between halteridium and human malaria (or even proteosoma). In the first, the numerosity of the infection remains fairly constant; in the latter, it varies within considerably wide limits. In the former, it is always above the vanishing point. In the latter, it is above it only during the febrile periods, below it during the apyrexial ones—there are alternating periods of profusion and paucity corresponding with the alternating periods of conflagration and quiescence of the fever and its incidents. A case of paludism removed to Europe may have occasional attacks of fever for years afterwards; during the attacks the parasites are found; between them none can be observed. By the hypothesis just given we may assume that during the apyrexial periods the parasites are really propagating themselves all the time in comparatively small numbers below the vanishing point. But what allows the occasional increase, and what compels the subsequent return to the normal condition?

We now approach the application of these remarks, which I fear have been tedious. The question is connected with several others. Since the parasites are capable of indefinite multiplication, what prevents them from destroying the host in every case of untreated infection straight off? On the other hand, what produces spontaneous recovery in so many cases?

These facts demand a reply. There *must* be some natural force which restrains the multiplications of the parasites in cases where death does not occur; and there *must* be some natural force which finally exterminates the invasion in spontaneous recovery. The existence of such a natural force is not a hypothesis; we are forced to admit it.

In short, we are confronted by the same problem as we find in the case of many bacterial infections. Like the bacteria, these protozoa demand our recognition of some force which makes head against them.

We can only ask, what is the nature of this force? It must be either some quality inherent in or produced by the parasites themselves, which checks their over-production; or some power generated in the body of the host which opposes them. Asexual modes of reproduction, such as we believe these parasites to possess in the human and avian hosts, are thought to tend toward spontaneous extinction; this may afford one explanation of the facts. Or the parasites may fabricate some chemical product noxious to themselves. Or the tissues of the host may acquire some principle of immunity. Or all these forces may act simultaneously.

On the whole, spontaneous decay of an invasion cannot be the only cause for its restraint or extinction. It is difficult to explain on this hypothesis such cases as the one referred to, where the infection lasted for years after the patient removed to England. The hypothesis implies also that all infections, severe or mild (i.e., *numerically* severe or mild) will recover at about the same time, and that the condition of the host will not be a factor in the recovery. This can scarcely be admitted.

As a matter of fact, the total sickness produced by a parasitic invasion must depend on several factors, such as the virulence or harmfulness of the species of parasite, their numbers, and the resisting and healing powers of the host. We can easily attempt to represent this relation numerically in a simple manner. The total sickness (s) may be considered as the difference between the mischief (m) caused by the parasites and the extent to which this mischief is healed by the system (h); or $s = m - h$. Again, the mischief caused by the parasites (m) varies directly as their virulence (v) and the number in which they exist (n); or $m = vn$. Lastly, the number of the organisms (n) varies directly as their prolificness (p), and, inversely, as the resistance (r) which they experience in living: or $n = \frac{p}{r}$. Combining these equations we obtain—

$$s = m - h = v\,\frac{p}{r} - h = \frac{vp - hr}{r}.$$

Here vp represents the total *morbific energy* of the invasion, while hr represents the total *resistant energy* of the host—the power of healing (h) multiplied by the power (r) which checks the multiplication of the parasites. If vp increases to excess while hr remains constant, s becomes correspondingly large, and death ensues. If, however, vp exactly equals hr, the sickness vanishes—the point of toleration is arrived at.

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The same equations must apply to all conditions of parasitism, animal or vegetable.*

The last result is of special interest here; if a point of toleration is reached the resistant energy of the host must be exactly equal and opposite to the morbific energy of the infection.

Again, from the first two fundamental equations we get, $s = vn - h$. At the point of toleration $s = o$, and we obtain, $n = \frac{h}{v}$; that is, the number of parasites which can exist at the point of toleration varies inversely as the virulence of the species of parasite; which is just the idea suggested by a comparison of halteridium, proteosoma and human malaria.

The co-efficient r represents the power of the host to inhibit the multiplication of the parasites—that is, the degree of immunity possessed by him. It is really a very complex quantity depending partly on the duration of the infection, tending to increase with that duration, and to decrease again after the infection has passed off. The study of it belongs specially to the new and important science of Immunity.

It is now necessary to apply these considerations briefly to human paludism. We may suppose that the first parasitic invasion begins with a rush, before the system has had time to bring its resistant energy into play. As, however, this energy begins to act, the invasion is repulsed (unless death occur) and driven back to or below the point of toleration. Perhaps if the resistance be strong enough, the parasites are exterminated then and there, and we have spontaneous recovery. If not, the parasites remain in small numbers; a few, perhaps the hardiest of them, being able, like other living things, to struggle on in an unfavourable medium. Presently the energy of resistance relaxes (as it is known to do in other infections), or is weakened by chill, fatigue, and so on. The parasites increase again in numbers. A second severe invasion accompanied by a recrudescence of fever ensues, to be followed by a second establishment of partial immunity. The history repeats itself; several similar attacks follow; and we obtain the picture of a typical case of untreated malarial infection.

Now, it is obvious that this state of things cannot continue for ever. Each attack has a sensibly pernicious effect on the host; anæmia, congestions of the organs are established. The system must make some final effort to obtain the mastery and to exterminate and not only reduce the invaders. It is probable that the energy of resistance increases with each successive attack, and that each attack becomes weaker and weaker in consequence. Lastly, the parasites can no longer make head; the medium becomes intolerable for them, and they die out altogether.

Such appears to me to be the true history in untreated paludism. The infection is a continuous one; the successive conflagrations of fever and periods of quiescence are due, as it were, to the swinging to and fro of the tide of conflict between the opposing forces of the host and the invaders; final extinction of the invasion occurs when the former gain the victory.

This is somewhat more than hypothesis; we are compelled to admit that something of the kind occurs. Otherwise recovery in untreated cases would never take place.

I have just referred to the fact that sparrows infected with proteosoma by the bites of mosquitoes threw off the infection much more readily in December than in July and August. This suggests that their energy of resistance is greater in the cool season. Another experiment made in August last suggests that one attack of proteosoma confers some immunity against a second. Five sparrows, each containing a very few parasites, were subjected to the bites of some old infected mosquitoes [2]; after the usual incubation period of five to eight days, four of these birds showed a new infection characterised by the presence of numerous young parasites. This new invasion was much more copious than the original infection, but still it never showed the enormous numbers of parasites found in *all* the originally healthy birds infected in this manner. I had hoped to repeat this experiment in order to obtain greater

* *Note*—Of course, these equations are of the roughest; the correct ones are differential equations, involving the independent variable *time* and requiring various integrations. It is scarcely necessary to go into such detail here.

certitude, but have found it impossible to do so in the cool season in time for this report.

According to many writers malaria is one of those diseases in which individual immunity is not developed. I think that this is a mistake; and a mistake which has risen from confounding the ordinary recrudescences of fever with fresh infections—it is thought that each recrudescence is due to a new invasion, and it is therefore naturally inferred that the preceding attack has conferred no immunity. This is a wrong conception of a malarial infection. Such an infection, if left to itself, normally develops successive recrudescences which are only a part of the original invasion. Looking at the subject in this light, I think we are bound to admit that temporary individual immunity may be finally established, either after an extremely severe single attack or after a long pervasion of the blood by the parasites. It is difficult to see how, apart from treatment, recovery can ever occur without it.

30. Conditions favourable to the Early Extinction of the Parasites.—Since it is possible for the invasion to become extinct after a certain lapse of time, we may now enquire the conditions most favourable to this. I have already suggested an answer. In paludism, as in other diseases, the energy of resistance is likely to vary directly as the morbific energy of the invasion. In other words, the more severe the initial infection, the more vigorous must be the reaction if death is not to ensue.

The system finds itself confronted with a life or death struggle. All its powers are roused; either the host or the parasites must perish.

In a mild attack the forces of defence are not sufficiently roused—the invasion is repulsed, but not extinguished. In a severe infection, when very existence is threatened, they are roused to the utmost; if they be successful the invasion is not only repulsed, but the impetus of the defence suffices to destroy the invaders completely, or very nearly so.

We have been made quite familiar with this fact by the multitude of experiments for the preparation of antitoxin and antivenine. Unless an animal be treated with a sufficiency of the toxin or venin, its blood does not produce a sufficiency of the antidotes.

This result may seem paradoxical. The general experience is that the worse the infection the less are the chances of recovery. Precisely; but we are forgetting the condition always implied by those theories. I say, *if the defence be successful* it will be more likely ultimately to extinguish the invasion in a severe than in a mild attack. Of course, in the former, before the system is fully roused to its danger, the parasites are more likely to win the victory immediately, the defence is less likely to be immediately successful, death forthwith is more probable. Again, we must not forget that the parasites produce a secondary effect on the organs which must, *cæteris paribus*, vary in degree directly as the violence of the infection, and which may cause death ultimately after the actual extinction of the parasites themselves. These various issues must be carefully kept apart.

What are the actual conditions, then, which are most favourable to the early establishment of immunity? The virulence of the parasite, the numerosity and repetition of the infection, and the *absence* of treatment.

It will be seen at once that all those conditions are exactly those which obtain among aboriginal populations living in very malarious localities. They are subject to virulent parasites; the number of parasites acquired in one infection is likely to be greater in a very malarious locality than in a less malarious one; the chances of repeated infection are greater; while such patients seldom take quinine.

The patients are not necessarily infected on one occasion only, but possibly over and over again for days or weeks. They are even possibly open to re-infection from themselves. To take an illustration from proteosoma of birds—I have just stated that sparrows were infected and re-infected by mosquitoes. Now, mosquitoes do not bite only once or twice; nor do they live only for a few days. They may certainly live for a month, probably in the same house or tree, and will continue to feed themselves every two days or so, according to the temperature. The same bird may become infected over and over again by the same mosquito. If the bird has an original infection, the mosquito may become infected from it, and after a week or so may infect it again with a worse infection. In this manner the bird may, so to speak, re-infect itself, by the mediation of the

mosquito, *from itself*. We do not know whether the laws of proteosoma apply entirely to human malaria, but if they do, as is extremely probable, the same thing will occur to human beings.

At all events, it is clear that poor people living in the humblest of houses in pestiferous surroundings are just as likely to receive infection on many days in succession as on one day; if the poison be present there is no reason why its action should be limited to one occasion. A European coming to such a spot, say for one day, contracts only a single infection; the inhabitant a series of infections. The former, mildly invaded in the first place, breaks the force of the invasion further by quinine; the latter has nothing to rely on but the reactionary vigour of his own constitution, which moreover must deal with a much more grave condition of affairs. In the former the natural forces which make for immunity, strongly aided by medication, are scarcely called upon to exert themselves at all; in the latter they must put forth their full strength, and that at once, in order to avert the great danger which threatens. In the first case, the parasites find little natural impediment to their indefinite propagation; when, on the occasion of a chill or of the temporary remission of quinine, they multiply again sufficiently to cause a slight attack of fever, the drug is resumed and their numbers immediately vastly reduced; and this state of things continues for years, perhaps with little inconvenience to the patient. In the second case, however, they are confronted very soon by a violent natural antagonism which they themselves have roused; which, if they do not succeed in overcoming it at once, gains vigour with their continuance and finally exterminates them.

Add to the second case the terrible secondary destructive effect on the organs produced by the first great rush of the invasion and we have elaborated the antithesis suggested in paragraph 26 between the continued paludism of Europeans and of Natives of tropical malarious localities.

In the first, we have the parasitic pervasion of the system continuing for years, now increasing now diminishing, attended by alternating periods of quiescence and of the conflagration of the typical fever, and producing only a moderate secondary affection of the organs.

In the second, we have the first inordinate rush of parasitism, followed, if not by the death of the patient, then by the speedy extinction of the invaders, and leaving behind it as a residuum an early and often severe affection of the organs.

Of course, such an antithesis can only be accepted in the rough and is often obscured by other considerations. The European, for instance, is generally more susceptible to the toxic effects of the parasites than the Native is, so that he seems to suffer more with less occasion. But a little reflection will suffice to disentangle these issues.

31. Influence of Difference of Species in the Parasites.—We now emerge on what is perhaps more solid ground.

Since the investigations of Golgi in 1885, it has generally been accepted that there are at least three different varieties or species of the parasites of malaria. They differ from each other morphologically and in their effects on the host; and these differences have been carefully mapped out by a host of observers in most malarious countries—until we can now distinguish one species from another almost at a glance. What effect may this difference of species have on the questions under discussion?

It is necessary first to consider that a great authority—Laveran himself—while admitting the morphological differences, refuses to admit that they constitute difference of species. He thinks [25, p. 84] that difference of climate or temperature will account for the morphological differences met with; and Marchoux, in his recent study of paludism in Senegal [22], supports this view. Laveran implies however, (p. 81), that if the various forms could be found exclusively, each at a separate spot in the same climate and at the same season, this would suffice to establish difference of species.

My own conviction, based on my experiences in India, is that this is exactly what occurs. In Secunderabad in the Deccan I made a very long study of fever during the rains of 1895 and of 1897, occurring in my regiment stationed in the locality called Begumpet. Though I found the parasites in some hundreds of cases, and though I observed scores of cases infected by the tertian

and by æstivo-autumnal parasites, I never once detected a single quartan parasite in a case of fever contracted in that spot. Nevertheless, it was easy to obtain examples of these parasites simply by going to the next regiments situated a mile or two away in the cantonment—at the same season and in the same climate, be it noted. Again, at Bangalore, from October 1895 to March 1897, I observed only the tertian and æstivo-parasites again. Not a single case of quartan was found in the station itself; and, moreover, all the cases of tertian came from one limited part of the town. It is impossible to explain these facts—of which I am quite sure—on any theory attributing the morphological differences to climatic ones. In Madras, according to Sturmer [35], quartan parasites abound. In the Sigur Ghât I found only quartan and æstivo-autumnal; and the same precisely at Kherwara, Rajputana. Hence the prevalence of the different varieties must vary according to locality—even when the localities are very contiguous.

In my experience, moreover, two forms are so rarely found together in the same patient, especially in recent infections, and so seldom succeed one another in him, that when such things occur they are much more reasonably explained by the hypothesis of mixed infections than by that of climatic influence. It is difficult to see how external climatic changes can alter the morphological characters of the parasites more than those of the red and white cells of the blood; while it is a pretty general biological law that morphological differences imply specific ones. It is frequently argued that the types of fever said by Golgi and Marchiafava to be associated with the types of the parasites are not rigidly observed in connection with them. All I can say is that I have generally found this association in recent infections; but that the study requires great thermometric and microscopical care—which is not always given—in order to avoid errors due to the presence, appearance or disappearance of parallel generations, to the use of quinine, and, possibly, to the existence of secondary fevers.

On the whole, I have personally felt it necessary to abandon all doubt regarding the existence of plurality of species. Further than this, as I stated long ago [23], I find in India exactly the same specific characteristics in the parasites as the Italians and others have done elsewhere. Murray, in his admirable little monograph [34], records the same experience.

It has often been thought that the parasites of birds are all forms of the same polymorphic organism. My cultivations of proteosoma in grey mosquitoes appear to set the question at rest, because I have always failed hitherto in cultivating the other forms known as halteridium. Proteosoma produced by me in sparrows, weaver-birds and a crow, by the bites of these mosquitoes, had always precisely the morphological characters of the original proteosoma from which the virus was obtained.

I must now go further, however, and note that while morphological difference is almost enough of itself to imply specific difference, we have no justification for assuming that morphological similarity, or even identity, implies specific identity. Two organisms may be closely alike yet may be really quite different. Thus, there may be many quartan parasites morphologically identical yet specifically distinct; producing perhaps distinct secondary effects on the human host; differing in virulence and, may be, in details of their life-history outside the human body. This possibility appears to have been generally lost sight of. We know, for instance, that many local fevers appear to differ largely in their secondary effects on the patients, some producing hæmoglobinuria, others diarrhœa, others having a peculiar incidence on the liver or spleen, and so on; although the microscope seems invariably to disclose only the three known morphological types. Again, according to many writers, there are two if not three varieties of the æstivo-autumnal parasites, though all are very similar in form. Such considerations suggest that each morphological type covers many really distinct species; that, in short, these types imply not only specific but generic difference; that each genus contains many distinct species, indistinguishable from each other under the microscope, but really possessing subtle differences in other respects. At all events, we cannot definitely say that such is not the case, or even that such is improbable.

Considering, however, the three readily distinguishable varieties—the quartan, the tertian, and the æstivo-autumnal parasites—let us see how the presence of

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one or another of them in a patient can affect the question of the disappearance of the parasites and the black pigment from his system.

In one very important particular. We know that when, from any cause, an attack of fever due to the quartan or tertian parasites ceases, the organisms disappear, apparently, from the blood in a day or two. This is not exactly the case with the æstivo-autumnal variety; here the fever-producing forms disappear as in the other cases, but a crop of crescents is produced which remains and is found in the blood for weeks or even months after the subsidence of the fever, but which seems to cause no symptoms. In the former case, with the partial or complete collapse of the invasion, the black pigment must cease, partially or completely, to be deposited in the organs. In the latter case, however, the crescents remain, as I have said, for a long time, and as they die one by one their pigment, which is always profuse, continues to find its way to those organs.

Now, we may conjecture that the elimination of black pigment must go on continuously with its deposition. I have already cited authority to show that it may be completely eliminated in a few months. As a matter of fact we often find less pigment in the organs of long infected birds than can be produced by a few generations of the parasites present. Bignami has studied these processes with great care and describes the course of elimination. Unfortunately I have not obtained his work yet, and therefore cannot quote from it; but Thayer gives an excellent summary [27, p. 225]. The period of elimination is, of course, not exactly definable, as it depends on the amount of deposition; but it probably may not, in some cases, extend beyond a few months. (See case 17 for instance).

In æstivo-autumnal infections, then, we may expect to find both parasites (crescents and their derivations) in the blood, and melanin in the organs, longer after each conflagration of fever, and perhaps after the final extinction of the parasites, than in the case of quartan and tertian infections. (It should, of course, be noted that crescents are practically encysted organisms, probably serving a purpose outside the host, and, when once formed, little amenable to the influences of immunity.) It follows, therefore, that in quartan and tertian infections occurring among aboriginal populations of malarious localities, the condition found by me in kala-azar, namely, one of absence of parasites and melanin, must be arrived at sooner than in æstivo-autumnal infections.

An interesting illustration of these observations is given by Captain Harold Brown's study of kala-dukh in the Purnea District [16], already referred to in paragraphs 9 and 13. He found parasites in 45 out of 50 cases; but in 43 out of those 45 crescents were present. It is clear, then, that these were cases of æstivo-autumnal infection. In my 75 cases, crescents were observed only in three. Hence, on the supposition that kala-azar in Assam is paludism, we may explain the discrepancy between Brown's results and mine, and at the same time give one good reason for the absence of parasites and melanin in the later cases by attributing them to a quartan or tertian infection. I may add that Rogers also failed to find crescents in his cases. In a letter to me Captain Brown adds that his investigations were made in April 1898, and remarks —"As a rule, the parasites were few except in the two cases that were noted as having quartan ague, in whom they were decidedly numerous. In the more recent cases, they were more numerous than in the chronic ones when, at times, it required patient observation to detect them." Crescents as well as "large and small pigmented bodies" were present in the two quartan cases; which, therefore, might have been mixed infections. Unfortunately, Brown does not specify the exact nature of the "pigmented bodies," which he refers to in most of his cases, and never refers to unpigmented amœbulæ, which are the fever-producing forms of the crescent-bearing (æstivo-autumnal) species. I gather, then, that most of his pigmented bodies were crescent-derived spheres, and that kala-dukh in Purnea is essentially æstivo-autumnal paludism.

It is possible to imagine that had the crescents been, so to speak, removed from Brown's cases, they would have exhibited the absence of parasites and melanin observed by me in kala-azar.*

* *Note.*—It is also possible that certain local varieties of æstivo-autumnal parasite may produce very few crescents. Thus, Dr. Daniels informs me that in British Guiana, though the species of parasite is æstivo-autumnal, he finds comparatively few crescents. He expressed his surprise at the number of those bodies in four Calcutta cases, although from my experience I considered them to be not at all remarkably numerous. It should be noted also that in British Guiana it is the rule to find enlarged spleens without melanin—so that the fevers there and at Nowgong seem to accord in several particulars, namely, the paucity of crescents, the frequent absence of melanin, and the low fever. See Appendix A 6.

The frequent discovery of crescents in kala-dukh appears to me, in the light of my experience of paludism among natives, to be rather remarkable. In my regiment at Secunderabad almost all first attacks of æstivo-autumnal fever were followed by crescents if large doses of quinine had not been given; but as second and third attacks developed the crescents always tended to become less numerous. Attention to the subject was forced on me by my researches on the mosquito theory, which require crescents for various experiments. I have attributed this to the gradual establishment of immunity which, though it can scarcely affect the full-grown organisms, may inhibit their formation, especially if, as Mannaberg thinks, they are due to syzygies of two young parasites in one corpuscle. Many of the æstivo-autumnal cases at Nowgong gave no crescents. In some of them this may have been due to quinine; in other and older cases, such as cases 16, 23, 24, 36, 38 and 44, their absence can scarcely have been caused by this. Season may have something to do with the matter—Brown's researches were carried on in April, mine in autumn. But I am certainly of opinion that with poor natives of India, the older the case the fewer are the crescents as a rule.

Another point also may have an important bearing on the questions at issue. Mannaberg has suggested the existence of an æstivo-autumnal parasite, the fever cycle of which is entirely unpigmented, and Marchoux depicts unpigmented sporulating forms in his paper on Senegal fevers [22]. If crescents ceased to be produced in such fevers, the inference is that all black pigment would cease to be formed. In Nowgong, however, I found no unpigmented sporulating forms in the spleen.

I think, then, that we may safely conclude that with an unpigmented quotidian, or a parasite producing few crescents, or an ordinary tertian or quartan parasite, the melanin is likely to disappear earlier than with the remaining varieties.

32. Secondary Effects of the Invasion.—I propose to deal very shortly with this point. As a matter of fact, we have little knowledge of the precise cause of many of the phenomena attending the invasion. The exact nature of the toxin (if there be one), that of much of the anæmia present and of the enlargement of the organs, cannot yet be considered as entirely elucidated; though, of course, many reasonable inferences, such as the irritation of the organs by the yellow pigment, have been drawn.* Putting etiology aside, the association of anæmia, enlargement of the spleen and liver, and so on, with paludism is one of the best known facts in medicine; to these symptoms, epistaxis, darkening of the skin, œdema, first of the feet and then of the face, ascites, dilatation of some of the superficial abdominal veins, progressive emaciation, and the frequency of inter-current attacks of diarrhœa, dysentery, cancrum oris, pneumonia, and so on, must be added. All these, symptoms of kala-azar, are recognised everywhere to be also symptoms of paludism and, therefore, need not all be examined here. A word, however, remains to be said on a point or two.

I have already mentioned that the *enlargement of the organs* in the worst cases of kala-azar seen by me, was not more extreme than in some cases of paludism seen in other parts of India. It is not so much the extremity of the enlargement found as the constancy of great enlargement in all established cases, which seems to be one of the leading features of kala-azar. *Primâ facie*, however, this is only a question of degree. See also Rogers [4, page 41].

I agree with other observers that extreme *anæmia* is not necessarily a leading symptom of kala-azar and that, when it occurs, it suggests ankylostomiasis as a complication.

Practically only the *low fever*, which is certainly not *generally* recognised as a symptom of paludism, remains to be considered. I have cited (paragraphs 26 and 27) Vandyke Carter, Kelsch and Kiener and Daniels, to show that such a thing really may and does exist in what is thought everywhere to be paludism. We must now endeavour to explain it.

In my cases of kala-azar it was obvious that, apart from the absence of parasites and melanin, this fever was not being caused by the actual parasitic invasion—the curve was not a malarial curve.

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* *Note.*—I have often thought that melanin may be more nearly concerned in those processes than is imagined. At the moment it is set free, the access begins, and when it is taken up by the phagocytes the fever ceases; while it is just those organs where it is most largely deposited which are the seat of future trouble.

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In my experience of true parasitic fever amongst the natives of India—that is, of fevers during which the fever-producing forms of the parasites are found in the blood—the amplitude of the curve is almost always large, and consists of about eight or nine degrees—say from 96°F. to 104° or 105°F. Even when this fever assumes a remittent character, the temperature still occasionally drops suddenly to a point some distance below normal, to be often followed by as sudden a rise to a high point preceded by a rigor or a chill. Of course, in a typical intermittent fever this occurs with the classical periodicity.

Again, in true parasitic fever the pyrexia does not continue indefinitely. After lasting a week or so, during which the fever-forms of the parasites are found in the blood, it ceases and is followed by an indefinite period of apyrexia, during which the morning temperatures are particularly low, though there are frequently small oscillations in the evening to just above 99° or so. At this stage no fever-forms are found as a rule. Another attack follows in a short time ; and the early history of a case of paludism is made up of such periods alternating with each other.

Thirdly, in parasitic fever, quinine has a marked effect.

In natives of India, among whom malarial remittent fevers are not very common, an early morning temperature above 98°F. generally suggests that the fever is not due to the parasites.

Now, in the low fever described in paragraph 6 and figured in Appendix C, we have very different characteristics. The amplitude is not large, and lies between about 99° and 102° only ; the morning temperatures are not often below 98° ; and every day, for weeks and months, we have an almost exact repetition of what occurred on the previous day ; while quinine—at least in a few large doses—appears to have no effect whatever.

There are, of course, some variations. In several charts, for instance, the morning temperatures were often decidedly low ; but the other characteristics—the small amplitude, the diurnal regularity, the intractability to quinine—remained.

Now, regarding the cause of this fever—its general characters,as well as the apparent absence of parasites, differentiates it sharply from the parasitic fevers. On the other hand, the curve is exactly that of low fever due to moderate local irritations, inflammations or congestions.

What local irritations or congestions were present in the Nowgong cases to account for fevers of this type ? Kelsch and Kiener have already supplied an immediate answer—the condition of the liver and spleen, perhaps of other organs.

Looking at such cases as they stand, putting aside all thoughts of any parasitic invasion which may have existed at an earlier period, and fixing the attention only on the enormous and often tender enlargement of the organs, we may ask, have we any right or justification for assuming that such grave local lesions should not be associated with a low fever of the kind described ? Certainly not ; any experienced physician will say that such fever is just what we would expect to find in association with such lesions, however these lesions may have been produced. It is almost impossible to conceive such lesions to exist without considerable febrile reaction ; and if we were asked to define the probable character of this febrile reaction we should, in reply, draw a chart precisely similar to those obtaining with the kala-azar cases—a small amplitude, a somewhat raised morning temperature, a long and regular continuance, and resistance to quinine.

In short, Kelsch and Kiener describe and explain the fever in a word—in the name they adopt for it—*la fièvre symptomatique.*

It may be said that this is no explanation ; that we require to explain why an enlargement of the organs produces fever. I fear I cannot attempt an answer. A secondary bacterial infection may be suggested. For my present purpose it is sufficient to point to the existence of this fever and to its apparent association with enlargement of the organs. Whatever it may be exactly due to, the fact of its occurrence remains a very important one in respect to treatment ; and I therefore invite a closer attention to it than appears generally to have been given it.

We do not even know the precise cause of the enlargement of the organs in paludism. Kelsch and Kiener would attribute it to the yellow pigment or to

the ferruginous deposits; but many cases of enlarged spleen occur in which there is none of either. It may, perhaps, be due to, or at least initiated by, the black pigment, or by a toxin secreted by the parasites; but, here again, there is evidence to show that the organs continue to enlarge without the presence of melanin, showing that the malarial invasion is already a thing of the past. Lastly, it may be due, as Manson suggests, and as the concurrence of the low fever may encourage us to believe, to a secondary bacterial infection; or perhaps it may be connected with the establishment of immunity, which is possibly part of the function of these organs—they may enlarge in the effort of producing the "internal secretion" of an antitoxin.

I have not laid much stress either on the yellow pigment or the iron, chiefly because our knowledge of both is very imperfect. The fact, however, that they are so frequently present in kala-azar appears to limit the malady to the small group of hæmolytic diseases, and is, therefore, valuable evidence in favour of the malaria theory. But I should add that Dr. Daniels is of opinion that both are produced in ankylostomiasis—Appendix A 6.

I will conclude this long discussion by formally considering the final question which still requires an answer—that of paragraph 28.—What proof have we that the condition of enlargement of the spleen and liver without black pigmentation, found by me in some of the cases in Nowgong, is due to malaria at all, and not to some quite different cause?

I have suggested an explanation of the phenomenon frequently already—that the parasites become extinct and the pigment is eliminated, leaving the organs in the condition referred to.

But since the melanin is absent, how be certain that it was ever there at all?

Daniels finds the same condition in British Guiana, and it probably exists widely elsewhere. May it not be due to a non-malarial disease which, however, has been mistaken for malaria?

On the whole, I think it is impossible to admit this, for the following reasons:—

1. The enlargement of the organs in Nowgong and British Guiana is an *endemic* enlargement. Now this, in general experience, is found only in malarious, even only in very malarious, localities.

2. The organs are seen to enlarge under our eyes in acute cases of paludism in which the parasites are actually present; and the parasites may often still be found when a considerable degree of enlargement has been reached.

3. The structure of the organs in cases in which the melanin is absent is identical with that in the cases where it is present; and cases of the former exist side by side with those of the latter, being like them in every respect save in that of the pigment.

4. All the cases give the same history of the typical fever and other symptoms of paludism.

There is, then, no reason for supposing that the cases without black pigment differ in nature from those with it, and no likelihood that this is the case. On the other hand it is easy to explain the absence of the pigment simply on the ground that it has been eliminated shortly after the extinction of the parasites.

Practically the only argument which can invalidate this reasoning is to the effect that the melanin once deposited, must remain permanently in the organs for at least a year or two *in every case*. I know of no grounds for such an assertion. It is even doubtful whether it can remain for long in any case.

If melanin can be eliminated in one case it can probably be eliminated in all, or at least in a percentage. The time required for its elimination must depend, *cæteris paribus*, on the amount of the deposit.

In short, before we can accept that the condition under reference is not due to malaria we must be in a position to prove that melanin cannot be eliminated at all except after some years.

33. Summary of the Discussion.—The objections to the malarial theory of kala-azar were stated in paragraph 22. They were (1) the high death-rate of the disease and its intractability to quinine; (2) the absence of parasites and pigment and the existence of low fever in the later stages; and (3) its communicability.

The first objections (1) were shown not to be serious ones (paragraph 24).

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The next objections (2) have been discussed at great length. Evidence from Kelsch and Kiener and Daniels was given to show that the melanin (and consequently the parasites) may disappear early, and that the condition of enlarged organs without melanin exists in other countries besides Assam; and citations were made from these writers and from Vandyke Carter to shew that a secondary fever may exist in connection with this condition (paragraphs 26 and 27). An attempt was then made to explain these phenomena from the point of view that they may originate in a malarial infection (paragraphs 28-32); and it was finally shown (paragraph 32) that the only *pathological* argument which remains against the malarial theory of kala-azar is one based on the supposition that melanin can never be eliminated except after several years.

In the absence of any definite proof of this and in the existence of some evidence to the contrary, I think that this argument, too, may be set aside.

The last objection (3) is an epidemiological one, and remains to be considered.

V.—The Epidemiological Difficulties Discussed.

34. Definitions.—It is generally thought that malarial fever is due to a poison generated in the soil, air, or water of certain localities, which are thence termed malarious localities. It is generally thought, moreover, that the disease is not communicable, directly or indirectly, from the sick to the healthy.

On the other hand, kala-azar is not connected with any one locality, and it is communicable from the sick to the healthy.

Hence, it is said, kala-azar cannot be malarial fever.

Let us examine the question.

I have admitted in paragraph 2 that kala-azar is an epidemic, and that it is "communicable from the sick to the healthy in some unknown manner." Let us first endeavour to define these terms more exactly.

A disease is said to be epidemic when it appears suddenly in a locality. Now, since diseases are not known to originate *ab initio* anywhere, this implies that the epidemic disease has spread into the locality from without—that it is a spreading disease. But it implies no theory as to the mode of spreading.

It is possible that a disease may spread in many ways: by the extension of some meteorological influence favourable to it; by the spread of some morbific element in the soil, air, water, flora or fauna of a country, from which it is communicated to man; or by communication, direct or indirect, from man to man.

In saying, then, that kala-azar is both epidemic and communicable, we state not only that it is a disease which is capable of spreading, but that we know at least one way in which it spreads—that of communication from the sick to the healthy. It will be advisable, first, to recall the evidence on which these statements were made, in order to be quite sue of their truth.

35. Evidence regarding the Epidemicity and Communicability of Kala-Azar Recalled.—The proof that kala-azar is a spreading disease is, I consider, quite sufficient, namely, that it has actually spread up the Brahmaputra Valley from the Garo Hills to the Nowgong District and beyond; the fact is attested by official statistics and by the statements of everyone who knows the locality. No discussion on this point is possible.

The other point is, perhaps, not quite so clear. As Sir W. R. Kinsey said at the discussion of the subject before the Royal Medical and Chirurgical Society [11, p. 820], it is difficult to prove the communicability of diseases that simultaneously affect a number of people.

It is proved in this case, however, by the facts, everywhere recognised, that kala-azar tends to confine itself to isolated villages, families and houses, and that it has frequently appeared in such after the entry of an affected person.

Had the disease spread by the extension of some meteorological condition it would have broken out everywhere at once; had it spread by means of some morbific influence slowly extending itself in the elements of external nature, it would not have moved by families and affected persons. If we accept the universal experience on the subject, which I think we are bound to do, we must also accept that the disease is a communicable one.

Hence, it now only remains to us to ask, is it possible that malarial fever is capable of becoming epidemic and of being communicated from the sick to the healthy?

36. Epidemicity of Malarial Fever.—As a matter of fact, epidemics of malarial fever—or at least of a disease extraordinarily like it—have been very frequently recorded. Thus Davidson [26, p. 146] says, "During the present century malaria has overrun the greater part of Europe on several occasions. We have first the epidemy of 1806-12; then that of 1823-27, which made itself felt over many parts of England and even in London; next came those of 1845-49; and 1855-60; and lastly that of 1866-72. Griesinger mentions, in addition to these, a considerable extension of the disease during the period of first invasion of cholera, namely, 1830-35.

"In Bengal we have records of more or less extensive epidemics of malaria in the following periods:—In 1807-9, reaching Southern India in 1809-11; in 1816, extending to Madras; in 1834, extending to Western Rajputana, Nazirabad, Neemuch and Mhow; in 1843-44, extending to Scinde, causing a terrible mortality among the troops in Hyderabad in 1843, and at Sukkur in 1844. This last outbreak reappeared in the monsoons of 1845-46. Epidemics, more or less extensive, occurred in 1850-51, 1863, 1866-67, the last corresponding with the European epidemy, and with the first outbreak of malaria in Mauritius. The disease was again epidemic in 1869-70 and 1878-79; in the latter years malaria was also widely prevalent in Mauritius, Madagascar, Cyprus, and even in New England. In the United States similar epidemic extensions have been observed during this century. The most recent one gradually extended over Connecticut, Massachusetts, Rhode Island, Vermont, and New Hampshire. During its prevalence in Connecticut it is recorded that enteric fever, from causing 400 to 500 deaths a year, so decreased that at the height of the malarial epidemic in 1879 it caused only 159 deaths. Whatever may be the cause of these outbreaks they are seldom directly to be traced to meteorological causes." The writer adds in a note, "A malarious fever is reported to have been recently epidemic in the Transvaal, carrying off more than 10,000 of the native population.—*Lancet*, May 27, 1893." He remarks further (p. 183), "The following are some of the points in which malarial fever in its epidemic manifestations differs from the endemic disease:—

"1. In regions where the tertian and quartan types are endemic, the quotidian type comes to predominate during the epidemic periods; and in those countries where the endemic fever is of the quotidian or double tertian type, these are replaced by the remittent and pseudo-continued forms; and fevers of short intervals, or of the remittent or continued forms, are most prevalent at the height of the epidemy.

"2. Pernicious attacks—cerebral and algid—become more prevalent in epidemic seasons.

"3. The destruction of the red corpuscles is vastly more rapid, and hæmorrhages, profound anæmia, and cachexia are established at an early period of the disease.

"4. In severe epidemics, adynamic and typhoid symptoms, the result in part of the anæmia, come to the front, and impart to them their destructive and fatal character.

"5. Natives, who are comparatively exempt from the endemic disease, suffer severely during epidemics."

Lastly, he says (p. 146) that, when epidemic, the disease may rise "to the intensity of the worst forms of pestilence." In Mauritius, out of a population not exceeding 130,000 in the area affected, the deaths in 1867 were 31,920."

Such facts appear to have been overlooked by those who consider Rogers' declaration that kala-azar is an epidemic malarial fever too portentous to be credible.

Rogers has given a very admirable description, [4] and [5], of the "Burdwan Fever" and other epidemics, drawing a parallel between them and kala-azar, based upon his examination of old records. He shows that fever, intermittent or remittent, enlargement of the spleen and liver, anæmia and dropsy, with a close of lung or bowel complications, were the symptoms; that the disease spread from point to point, and that it was communicated by sick persons to healthy ones. He gives copious quotations which show in the clearest manner

(see especially those from Dr. Jackson) that the disease was communicable and that it attacked members of the patient's family. It is impossible to read these excellent passages of Rogers' work without feeling convinced that the Rungpore and Burdwan fevers were identical in symptoms and epidemiology with kala-azar, kala-dukh, and kala-jwar, and that all alike were, or are, epidemic and communicable diseases.

But the point of all this argument may be turned, and in the case of Rogers' forcible parallel has been turned, by the criticism that all these so-called epidemics of malarial fever were in reality epidemics of other diseases, typhoid in Europe, ankylostomiasis in India.

In my opinion this criticism is quite unjustifiable. In the case of the epidemics in Europe and America, it ignores the fact that even before the differentiation of typhoid and ever since the days of Torti, the profession was quite able to distinguish between malarial and continued fevers. In the case of the epidemics of India and Mauritius it ignores the fact that the existence of the typical malarial fever and of enlargement of the organs was expressly noted. In short, it asks us to assume that the scores of medical men who had to do with these epidemics were most grossly ignorant of their profession, while it invites us to prefer to the opinion of these eye-witnesses the diagnosis of critics who certainly never saw the epidemics and who have probably never even studied the records of them. It is quite inadmissible, for instance, to declare that the Mauritius outbreak was really ankylostomiasis. I have studied some of the records of that outbreak. It was not ankylostomiasis, nor anything like it.

A much more reasonable criticism would be that these epidemics were not due to paludism, but to a disease symptomatologically similar to kala-azar to itself. It may be said that all these epidemics in various parts of the world were really instances of kala-azar which has long been spreading in various quarters, though always mistaken for malarial fever. But this begs the question – still to be finally considered—whether the diseases are identical or not.

Theories attributing the enlargement of the organs to a substratum of "general malarial taint" and the spread of the disease to some other cause, are always insupportable. I have studied in some of the most malarious spots in India, and, even in them, never saw any *general* enlargement of the organs approaching in degree that almost always found in kala-azar. As remarked in paragraph 5, any general malarial taint producing the state of things found in this disease would suffice in itself not only to decimate, but probably to exterminate, the population. No; we are obliged finally to admit that in all these epidemics referred to the epidemic disease is itself a single entity—a fever involving enlargement of the organs; and that in the later epidemics studied by Rogers this fever is also communicable from the sick to the healthy.

37. Is Malarial Fever Communicable?—But malaria is an emanation from the soil, it is a product of decomposing vegetation, it springs from water-logged areas, it rises in mists and exhalations, it is not communicable by sick persons.

This is the great difficulty felt in regard to these outbreaks by everyone since the days of Dr. Jackson.

The difficulty is met by this question—What sufficient reason have we for assuming that malarial fever in general is not a communicable disease?

I seek in vain for a reply—there is no sufficient reason.

What, precisely, do we know regarding the exact mode of infection of human malaria?—absolutely nothing.

The mode of infection of malaria—we find ourselves at a step in the midst of the malaria problem. I propose to deal very shortly with it here, because, as noted in paragraph 7, the study of the question concerns other duties of mine, apart from those extending to kala-azar. But I may endeavour to define our ideas on the point.

What do we know about the gross epidemiology of malaria?—very little. Its incidence varies according to locality and season; it seems to be connected in some way with dampness. That is about all. Similar facts are known about many diseases.

What about the exact mode of infection?—Only endless hypotheses—conduction by the air and the lungs, by water and the alimentary canal.

We know that the parasite must enter the body from without; but how, exactly, it does so remains a mystery which will only be solved when we have succeeded in finding its extra-corporeal stage and in causing experimental infection by means of these extra-corporeal organisms.

What makes us think that the disease is not communicable from the sick?

First, that people seem often to contract it in uninhabited wilds. Whether they really do so may, I think, be open to question. But admitting the plea, this gives only one mode of infection—namely, from the elements of external nature. It does not necessarily exclude other modes of infection, such as communication from the sick. A traveller enters a particular jungle or terai and acquires fever. He may certainly have acquired it from external nature; but what about the fever-stricken villages on his route, what about the sick servants he probably takes with him? Had he been carried alone in a balloon to the particular jungle, and been left there for some nights and had then been attacked by fever, the experiment had been of scientific value. A malarious locality generally implies malarious inhabitants. At the best, the one mode of infection does not necessarily exclude the other. Malaria may be communicable both from the elements of nature and from the sick.

Secondly, that patients in our hospitals and in their homes seem very rarely, in our experience, to spread the disease round them. Certainly; but the same—at least as regards hospitals—may be said of cholera, typhoid, or even of plague, which are yet, surely, communicable diseases. There is a question of environment.

Communicability may be direct or indirect. Scabies and venereal diseases afford examples of the former. But contagion, strictly speaking, is rarely the mode of communication; it is seldom that the infection is taken from the body of one person and placed directly upon or into the body of another. There is generally a medium—air, water, soil, excreta, insects, other animals. Each disease appears to require its special medium. If this medium does not exist, the disease cannot be propagated from the sick to the healthy.

As regards our malarious patients, they have probably been removed from the spot where they acquired the disease to our hospitals or their own homes, were the disease does not ordinarily exist. It is, now, no argument to point to the absence of infection of contacts, since, from the original absence of the disease from the place, we may reasonably infer that the conditions necessary to its propagation have never been present there. It is possible that if the observer had removed the case to another house in the malarious spot itself, where these conditions are presumably present, he would have found that communication does take place—that the patient's relatives and friends are attacked—just as in kala-azar. I need only refer to the similar difference of communicability of plague, cholera, or typhoid in sanitary or insanitary surroundings, respectively.

Such arguments, however, only weaken the case against communicability in malaria; what can be said definitely in favour of it? Three things.

(1) Paludism is a parasitic disease. Parasites must propagate themselves; and it would, therefore, appear to be necessary for them to pass from host to host. All parasites which have as yet been sufficiently studied do so. Are the parasites of human malaria to be exceptional?

(2) Malaria of birds (proteosoma) is communicable from sick to healthy sparrows through the mosquito [1 and 2]. Every step in this evolution necessary to the enquiry has been studied under the microscope, and numerous birds have been actually infected (paragraph 1).

(3) Some steps in the similar evolution of one, or perhaps two, of the human parasites have been made out; but the life-history has not been completed.

It should be added here that there are indications that proteosoma may be conveyed in a manner less direct than from an infected to a healthy bird [2], namely through the "black spores."

Frankly considered then, the reasoning which makes against paludism being communicable cannot be looked upon as amounting to the first order of scientific proof. The fact is that the epidemiology of malaria has long been in an extremely nebulous and unsatisfactory condition.

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On the other hand, I venture to state definitely that proteosoma of birds is communicable. Owing to the great similarity between the avian and human parasites, and to the fact that research in regard to the latter has already yielded results identical to a certain distance with those obtained in respect to the former, it becomes almost impossible to avoid a like conclusion for paludism.

In making this statement I do not wish to be misunderstood. The disease cannot be directly communicable like scabies or venereal disease; but rather indirectly like rabies, filariasis, Texas cattle-fever, or nagana. Accepting the analogy with proteosoma, communication will require that the proper species of mosquito, or perhaps other insect, be present, and also that the particular insect has lived for a week or more, after biting the subject, before it can infect the object. Now, mosquitoes have many enemies—spiders, bats, strong winds, while, so far as I can ascertain, the species of insect which commonly infest our houses in India, and the larvæ of which live in pots of water, garden cisterns, and so on, cannot carry human malaria. Hence it follows that very particular conditions must be present before communication can be established.

Such conditions are not likely to exist to any great extent in our hospitals and in the houses of Europeans. In the Nowgong District, however, the houses of the poor are placed in the most favourable situation in this respect. Situated on the ground, surrounded by pools of stagnant water, and made generally of open matting work, they permit the ingress of hordes of mosquitoes of numerous species which, day and night, bite the half-naked bodies of the inmates, and when gorged, sleep in the dark, damp corners of the roof, returning after digestion for another meal, and living on in the same house probably for weeks and perhaps even months.

It will be perceived that a mosquito of the proper species existing in such a situation may carry the infection from any sick person who has entered the house to many of the other inmates in turn; and that, moreover, as suggested in paragraph 30, most of the insects there may shortly become infected and may repeat the dose of malaria nightly to the unfortunate inhabitants until all suffer from a frightful condition of parasitism. Still further, many of the infected insects may escape to neighbouring houses and afflict the occupants of these in a similar manner. Finally, when a patient so attacked removes to another village or hamlet where the mosquitoes of the proper species exist, he will start an epidemic of the same nature.

It should also be remembered that, according to my observations on proteosoma [2], very few sparrows bitten by infected mosquitoes ever escaped infection, and that nearly all of them suffered from the severest invasions I have ever witnessed.

Some other attempts at the solution of the malaria problem should be mentioned here. Sakharov, Rosenbach, Blumer, Hamburger and Mitchell—see [27, p. 27]—have kept the parasites alive in leeches. MacCallum found his motile vermicules in the intestine of crows(?) with halteridium; but these birds suffered from echinostomes [39, p. 130].

Rogers, to whom we are so largely indebted for his work on kala-azar and especially for his boldness in declaring the communicability of paludism, does not, however, I think, afford a very satisfactory explanation of this phenomenon. He attributes it, in the case of kala-azar, to a heightened virulence of the parasites of malaria in that disease, and considers the path of infection to be by way of the lungs. It is little likely, in the case of an animal parasite, that any increment of virulence should suffice to change its mode of propagation; and he cites no experiments to prove communication by the lungs.

On the whole, I think that the mosquito theory of Manson will suffice to explain the whole epidemiology of malaria, and believe that it may be accepted as established, although many details remain to be discovered.*

* *Note.*—Just as I conclude this paragraph, I have heard, by the kindness of Dr. Edmonston Charles of Rome, that Grassi, Bignami, and Bastianelli have succeeded in confirming my results regarding the cultivation of the æstivo-autumnal parasite. They have produced the "pigmented cells" in the Italian mosquito called Anopheles claviger, Fabr., or Anopheles maculipennis, Meig. Dr. Charles has sent to me two specimens of this mosquito given him by Grassi. It is, however, different from my "dappled-winged" mosquito. These observers, writing in collaboration, have already published a preliminary note on the subject (40).

It should be added here, however, that I failed to propagate any of these parasites in Nowgong, although several species of mosquito were employed and much time was spent on the efforts. But there were few suitable cases for experiment, and most of these refused to allow it. Later, in October, the cold weather set in; and, in short, the conditions were not at all favourable for the work. The discovery of the particular species of insect required for each species of gymnosporidium will probably require special research in different countries or even localities, while it practically constitutes only a detail of the work on proteosoma. I have, therefore, preferred the attempt to follow out the life-history of this parasite, as a type for all the other varieties, to wasting my time over efforts to find the hosts of each one in turn. There is, I think, little doubt that all will have the same development in insects, that all will produce "germinal threads" and "black spores," and that all will be communicated by the bites of the definitive hosts. Moreover, I think it very likely that the infection of paludism is acquired only through the bites of mosquitoes (or perhaps other insects). Injection of the poison straight into the blood by means of the veneno-salivary gland of suctorial insects is a means of infection which, devised by nature herself, far exceeds in certainty, as well as in its beautiful adoption of the simplest route, the coarse and clumsy methods of propagation which human imagination has yet been able to suggest for malaria.

38. The Special Virulence of Kala-Azar.—If kala-azar be paludism, how explain its excessive gravity? I do not know whether we possess any satisfactory explanation; but we know that many diseases are specially virulent sometimes, less so at other times. Two factors may enter into the product which causes the heightened gravity of the disease — the specific virulence of the variety of parasite concerned, or its numerosity. In any epidemic of paludism we may imagine either that a new and peculiarly virulent species of parasite is passing through a country; or that the epidemic is occasioned only by one of the old parasites, which, however, now infects people in larger numbers than it formerly did. I need remark only on the latter supposition.

I have shown [1] that with mosquitoes fed, respectively, on sparrows with many and with few parasites, the former insects, as is to be expected, contained the greater number of organisms. It is to be presumed then that, on biting healthy birds, the former would also inject a larger number of "germinal threads" and produce severer infections than the latter could. Similarly, I know as a fact that mosquitoes which have been fed over and over again on infected birds finally acquire a vast number of parasites and give the most terrible infections to birds. In this way I can artificially increase, not exactly the virulence of an infection, but its numerosity. In fact, it might be possible to start a local epidemic of severe "proteosomiasis" by this means among sparrows. I should have to load a large number of mosquitoes with parasites by feeding them over and over again on few infected birds and should then release them. Every bird next bitten by these insects would, I know for a fact, suffer from very severe infections, and each bird would similarly propagate its severe infection to others. An epidemic of sparrows' kala-azar would possibly sweep through the place.

It is evident that with all parasites we cannot expect the number of them found in patients to be constant. In some localities, apart from sanitary differences, they are few; in others very numerous. This merely follows the general law of chance or probability regulating the occasional accumulation of phenomena in general. Thus, we may have epidemics of round-worms or ankylostomes. If these happen to accumulate, so to speak, in large numbers in any given locality, they will be propagated in all directions from that locality in larger numbers than from localities where there were originally only a few of them.

But, however we may attempt to explain the phenomenon, the fact remains (paragraph 36) that epidemics of paludism, or of a disease closely similar to it, have spread over various countries from time to time; so that there is nothing at all unusual, as some appear to think, in the present outbreak in Assam. The discussion then returns to the point from which it started – the pathological question – what is the real nature of kala-azar, and, by implication, of these frequent epidemics so similar to it?

VI.—Conclusions.

39. The Nature of Kala-Azar.—It will be advisable, before attempting to draw final conclusions, to separate the facts from the theories in the previous discussions. The *facts* appear to me to be as follows:—

1. Kala-azar is an epidemic and communicable disease (paragraph 35).

2. Its symptoms are very like those of malarial fever. In established, *i.e.*, fairly advanced, cases, the disease consists principally of considerable enlargement of the spleen and liver, accompanied generally by a low fever, a certain degree of anæmia, and other secondary symptoms. The history of such cases is always that the illness commenced with high fever, generally with repeated rigors; and that the organs began to enlarge after this fever had lasted some time (paragraph 6).

3. The death-rate is high; but recovery often occurs.

4. The disease is known to exist only in malarious localities.

5. In Nowgong, side by side with the cases of established kala-azar, there were numerous cases of typical early malarial fever, in which the malarial parasites were found in abundance, and which already showed commencing and rapidly increasing enlargement of the liver and spleen. There were also cases of a later stage of malarial fever, in which the organs were more enlarged and a few parasites were found; or in some of which, if no parasites could be detected, melanin could be obtained from the spleen (paragraph 18).

6. In cases of established kala-azar at Nowgong, the parasites of malaria were found in a few of the more recent ones, and melanin alone in the organs of a few more; but in many, including some autopsies, no parasites and no melanin at all could be detected In most of the last, both enlargement of the organs and low fever were present. Yellow pigment was found in a large number of the cases (paragraph 18).

7. Kelsch and Kiener state that melanin is often absent in cases which they describe as malarial fever, a few months after the beginning of the illness. Daniels states that in British Guiana the majority of enlarged spleens contain no melanin. Vandyke Carter, and Kelsch and Kiener describe a secondary fever, not due to the parasites, connected with malarial fever; and Daniel notes the existence of a similar fever in cases of enlarged spleen, even in cases when the enlarged spleen contained no melanin (paragraphs 26 and 27).

8. There is no evidence to show that melanin always remains permanently in the organs.

9. In seven autopsies on cases of established kala-azar, no difference could be detected between the cellular structure of the organs of cases in which melanin was absent and that of cases in which it was present. Fatty degeneration was generally absent (paragraph 18).

10. No evidence was obtained by me of kala-azar being due to any cause other than malaria (paragraph 18).

11. Ankylostomes were found in a considerable number of the cases of kala-azar examined by me (paragraph 18 .

12. Ankylostomes do not produce enlargement of the liver and spleen (paragraph 11).

13. Numerous epidemics of a disease thought to be malarial fever are on record (paragraph 36).

14. One of the malarial parasites of birds, proteosoma, is communicable from sick to healthy birds by the agency of the mosquito (paragraph 37).

15. The mosquito stage of one of the parasites of human malaria has been partially followed (paragraph 37).

These facts drive us at once to the following alternative:—

(*a*) Kala-azar is not malarial fever; but a disease macroscopically and microscopically similar, except for the absence of the parasites and melanin. If so, this disease exists also in British Guiana, and possibly in other localities; but only in localities where typical malarial fever abounds as well.

(*b*) It is malarial fever; in most cases of which the parasites disappear toward the later stages of the disease, and in a few cases of which the melanin also disappears at a still later period, leaving the

enlargement of the organs accompanied by a low fever. If so, the disappearance of the parasites and melanin occurs also in British Guiana, and possibly in other localities, and must be explained.

The *theories* attempt this explanation. They endeavour to show :—

1. That a malarial infection consists of a continued pervasion of the blood by the parasites, which, however, in normal untreated cases increase and diminish in numbers in alternating periods, corresponding with the alternating periods of fever and apyrexia (paragraph 29).

2 That this continued parasitic pervasion tends toward extinction, either by spontaneous exhaustion or by the gradual establishment of immunity in the host (paragraph 29).

3. That special conditions, especially those in which kala-azar occurs, are likely to accelerate this process of extinction of the parasites (paragraph 30).

4. That the species of parasite concerned is likely to influence the amount of melanin deposited in the organs and, therefore, the period in which it is got rid of (paragraph 31).

Reviewing the subject, we see that :—

1. The alternative (*a*) given above is exceedingly inacceptable. No observations of a disease exactly like malarial fever but in which either the parasites or melanin have not been found in the early stages on exhaustive examination are on record. It is highly improbable that two diseases should present such close pathological similarities, and that one should exist only within the boundaries of the other and yet be essentially different (paragraph 33).

2. The alternative (*b*) can be inacceptable only on one ground, namely, that melanin once deposited can *never* be eliminated under at least a year or so. In the absence of precise knowledge as to how long the elimination of melanin requires, we are not justified in admitting this (paragraph 33).

To come to a conclusion then :—

The probabilities against alternative (*a*) are very great ; but the only final objection against alternative (*b*) is one based upon a postulate which is not proved, and which is scarcely even probable.

Unfortunately, in the science of medicine we can seldom attain to the absolute proofs of the exact sciences, and when we say that a given issue is proved or disproved we must imply as a rule only that the probabilities for or against it are very large.

Speaking entirely in this sense, I am willing to say that I think alternative (*a*) must be abandoned.

I am, therefore, of opinion, after a very careful survey of the question—and, I may add, an entirely impartial one, so far as I am concerned—that though the objections to the malarial theory of kala-azar are serious enough to require minute scrutiny, they are not strong enough to withstand the numerous facts in favour of the theory. I think, then, with Rogers, that kala-azar is malarial fever.

40. The Pathology and Epidemiology of Kala-Azar.—Conclusions regarding details of the disease may be briefly added here.

I have already expressed my views of the symptomatology in paragraph 6. The course of the malady is divided into three stages, the characteristics of which are : —

Recurrent conflagrations of high fever with rapid enlargement of the spleen, and generally also of the liver in the first stage.

Great tumefaction of the organs with low fever in the second stage.

Cachexia, with gradual decrease of the organs, disappearance of the low fever, and, frequently, intercurrent attacks of pneumonia or dysentery in the third stage.

I think that the first stage is chiefly that of the parasitic invasion ; the second stage that of the secondary effects of the invasion ; the third stage that of the tertiary effects, namely, the result of the secondary effects.

Thus, the beginning and the end of the second stage should be marked by the beginning and the end of the low fever. At first we have only the manifestations of the parasitic invasion, consisting of repeated attacks of typical malarial fever ; gradually, as the system begins to feel the effect of the invasion on the organs, the low fever sets in ; finally, unless death has occurred, recuperation is attempted in the face of the conditions left by the previous stages.

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As far as I can gather, the low fever commences about the end of the first, second or third month of the illness; and it tends to cease, I think, in nine months or more from the onset of the disease. It is probable that the low fever sets in earliest in the severest infections.

It seems both convenient and accurate to select the low fever as the sign of the second stage; it is easily detected by the thermometer, and should represent the degree of the secondary effects, to which entirely, and not to the parasites themselves, I ascribe it (paragraph 32).

The parasitic invasion, however, probably lasts well into the second stage, ever decreasing according to its duration. At the same time the system feels the toxic effect of the parasites less and less; but suffers more and more from the residual condition of the organs and the low fever.

The melanin is, I think, constantly being eliminated as it is deposited; and some months after it ceases to be deposited, that is, after the invasion is exhausted, it is probably got rid of altogether in many cases. Judging from Case 71 this may be accomplished in seven months from the onset.

There seems to be a rapid fall in the number of red corpuscles after each parasitic exacerbation, with a corresponding recuperation afterwards; but in the second and third stages the anæmia seems to me to remain constant, being maintained by the secondary effects. Kelsch and Kiener note this in paludism in general. I fancy that the yellow pigment results more from the anæmia due to the secondary effects, than from that due to the parasites themselves.

Œdema may appear early in the second stage, but more commonly toward the end of it.

The end of the second stage, when the system exhausted after the severe illness lies prostrate to intercurrent affections, seems to be the most dangerous epoch. Now, too, if any considerable number of ankylostomes are present, they must begin to make themselves heavily felt. Death is actually caused in most cases by dysentery, diarrhœa or pneumonia; but in many ankylostomes and even other worms have played an important part in the final scenes.

I can give no evidence regarding darkening of the skin.

I was not able, in the short time at my disposal for the enquiry, to assure myself regarding the species of the malarial parasite which causes kala-azar, or even whether the disease is caused by a single species (paragraph 21).

Whatever species it may be due to, however, I conceive the disease to be a form of paludism in which the infection falls with a very heavy incidence on the spleen and liver, especially the latter. It is, in fact, the secondary symptoms —the enlargement of these organs and the low fever—which are the gravest feature of this disease and which, I think, are the chief cause of the exceptional mortality. It is well-known that in some localities and in some races the parasites effect these organs but little; in others much. Why this should be we cannot say. But the fact remains that kala-azar is principally a manifestation of the secondary results of malarial fever.

I will add here some remarks of Dr. Daniels on the sections examined by him (paragraph 17). "The minute anatomy," he writes, "shows merely evidence of a hæmolytic disease. Direct evidence of malaria, *i.e.*, black pigment, is wanting in some of the cases. If the hæmolysis, of which the yellow pigmentary deposits give evidence, be the result of malaria, this must be of some form in which the hæmolysis is quite out of proportion to the melanosis or direct product of the organism, and would, therefore, probably indicate a specific form of parasite differing at any rate in its chemical activities from that met with in British Guiana. The absence of fatty changes and the different disposition of the pigmentary and ferruginous granules prevent any support from the structure of the organs being given to the theory of ankylostomiasis."

It appears possible to me, however, that the evidences of hæmolysis referred to here are not so much the effect of a particular parasite with special chemical activities, as of the great secondary enlargement of the organs and the concomitant low fever. If these cause anæmia, as they most certainly do, they may be expected also to yield evidences of hæmolysis.

By such a theory the yellow pigment would be a result, not a cause, of the enlargement of the organs. In Case 75, for instance, the spleen was greatly enlarged, congested and tender; yet *post mortem* it was found to contain no

yellow pigment to account for its condition. But there was yellow pigment in the liver—which was little affected.

The epidemiology of kala-azar must be that of malaria in general, and is bound up in the life-history of the pathogenctic parasites. It is extremely probable that the life-history of the parasites of men and of birds is similar. Proteosoma of birds is communicable from sick to healthy birds through the agency of the mosquito ; but there is evidence in the existence of the black spores of a second more circuitous route for the infection—though it seems to me very likely that actual infection in malaria is produced only through the veneno-salivary gland of the insects.

Some steps in the mosquito stage of the human æstivo-autumnal stage have been followed in " dappled-winged" mosquitoes. So far as they went, these steps were exactly similar to the corresponding ones of proteosoma, strongly suggesting a similar history throughout.

It appears to me possible that other suctorial insects, as well as mosquitoes, may also carry the infection of malaria.

While, then, I am of opinion that malarial fever is a communicable disease, I think that it is only indirectly so—through insects—and that for communication it requires the presence of the proper species of insect. I think also that there is a second cycle the nature of which has not yet been elucidated.

While I consider, as I have said, that kala-azar is a form of malarial fever with a marked incidence on the spleen and liver, I must add that I think its mortality is considerably enhanced by the presence of ankylostomes and other intestinal parasites, and of dysentery in very many of the cases.

I must also guard myself against being interpreted to mean that malarial fever of this type is confined to cases of so-called kala-azar and kala-jwar. On the contrary, I think that isolated instances of a precisely similar fever occur more or less throughout India, and that in particularly malarious localities they occur in large numbers. As to why the disease should be more prevalent in some localities and why its prevalence now in Assam amounts to an epidemic, I can offer only conjectures (paragraph 38) ; but there is nothing in these facts to prejudice the view that the disease is of a malarial nature.

I think that kala-jwar in the Darjeeling Terai is practically the same as kala-azar in Assam.

VII.—RECOMMENDATIONS.

41. Professional Recommendations.—Kala-azar is a local disease; but it is a form of the most important of tropical diseases, malarial fever, and a form which is probably by no means confined to Assam. Hence the difficulties which it has presented appear to me to be of great and general importance. I have no doubt that a similar form of malaria, possessing similar points of interest, occurs widely throughout the tropics. And these points of interest are far from being merely academical, but are intimately bound up with questions of the proper diagnosis and treatment of malarial fever in general. I will now endeavour to show how this is the case.

Kala-azar is interesting for the following reasons :—

(*a*) The frequent complication by ankylostomes.
(*b*) The early extinction of the primary malarial invasion, and the subsequent elimination of the melanin.
(*c*) The heavy incidence of the invasion on the spleen and liver; and the secondary low fever.
(*d*) The communicability of the disease.

With regard to the *complication by ankylostomes*, so much excellent matter has been written by Rogers that I have only some isolated remarks to offer. I agree with him that kala-azar is not ankylostomiasis; but this does not imply that I under-estimate the importance of the worm in many cases of the disease, and in Assam generally as in other localities. These parasites were found in 11 out of 16 cases of kala-azar which were carefully searched for them ; and it was obvious that in several instances they amounted to a serious

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complication. In several, however, such as Case 75, none could be detected; while in others they were obviously present only in small numbers and were producing no discernible symptoms. I concur entirely with Rogers and others that when present in large numbers they produce a condition of severe anæmia which does not belong to kala-azar pure and simple, and which often suffices to show the existence of this complication at a glance. The two diseases are quite different; the one being a fever, with an early history of a sudden febrile attack, leading to great enlargement of the organs; the other being a slowly progressive anæmia, without enlargement of organs, but sometimes accompanied by slight fever (Daniels—Appendix A).

Hence, it might be thought that the differential diagnosis should be easy—at least, where the diseases exist in different persons. This, however, is not always the case—if we rely upon microscopical symptoms alone. It is true that malarial fever in its earliest stages of severe recurrent pyrexia and in its second stage of enlargement of the organs (if this exist) can scarcely be mistaken for ankylostomiasis. But in the later stages, where tumefaction of the organs has not occurred to any great extent, or when it has subsided on the establishment of cachexia (paragraph 6), and when the final anæmia and œdema of malarial cachexia are very marked, the diseases may certainly be easily confounded.

How much, then, must the difficulty of judging be enchanced when both the diseases exist in the same person—that is, when ankylostomes are present in the third stage of paludism? In the earlier stages of the latter, when we find the outbursts of typical malarial fever or the enlargement of the organs to be constantly attended by more anæmia than is usually associated with such symptoms, we are justified in suspecting the presence of ankylostomes at once. If, for instance, we are confronted by a case of excessive anæmia and dropsy, with marked tumefaction of either the liver or spleen or both and a malarial history, we can scarcely hesitate in ascribing the condition to both diseases. But later, when the epoch of the fever has passed, when malarial cachexia is pronounced, when the organs have subsided to their normal sizes, and only anæmia and dropsy remain as the final consequence of this cachexia—symptoms equally of ankylostomiasis—how are we to discriminate? How tell whether the condition is paludism simply, or paludism *plus* ankylostomiasis, or even the latter alone? Yet it is just at this stage when we are most urgently called upon to detect the complication if it exist, because it is just the stage of a malarial infection when ankylostomes are calculated to have the most fatal effect—when the system, already weakened by months of a severe illness, requires all the strength it can summon, and can least afford to support these debilitating entozoa.

Again, even in the earlier stages of paludism, when the ankylostomes, though present, are so few that they cause no visible anæmia, are we justified in ignoring their presence? On what grounds may we do so? Suppose the paludism to be severe and to threaten a critical third stage, when the question of recovery will depend on the final resources of the system, is it not necessary that these resources should be husbanded to the utmost from the first? The ankylostomes may be too few to occasion anæmia at this early stage, but may still make their presence felt heavily at a later one. If they produce no anæmia, how are they to be detected? In other words; are we justified in waiting for the entozoa to diagnose themselves, so to speak, by establishing an anæmia which will probably kill the patient?

This raises the general question of the proper diagnosis of ankylostomes. Are we ever justified in allowing these parasites to diagnose themselves in this manner? To wait until they have disclosed themselves by inflicting a grave, perhaps a fatal injury, when we have ready at hand the simplest and most certain method of detecting their presence, would seem to be one of the most inexcusable of doctrines and practices.

And this question does not apply only to Assam. It applies probably to the greater part of India, as the literature of the subject shows clearly enough [15, 17, 18, 19, 20, etc.]. The worms have a very wide distribution, and probably cause a monstrous mortality.

The pleasant and easy beliefs so sedulously repeated, that the worms are harmless, or that they are harmful only in large numbers, such as five hundred

or so, have certainly had a bad effect on tropical medicine. This has been noted by many writers, and the Sanitary Commissioner with the Government in India has referred to the matter frequently in his Annual Report—apparently without much influence on these unfortunate popular notions.

Such notions are merely part of that curious heresy that all parasites and "germs" are "harmless"— a most groundless belief, due to insufficient consideration of the subject. The correct professional attitude toward questions of this nature is that there is a *primâ facie* case *against* every parasite. Any and every species of parasite should, in the interests of our patients, be held to be harmful unless and until the contrary be absolutely proved; they are intruders, and, therefore, their capacity for mischief is at least a presumption which should be acted on in the absence of complete proof to the contrary. Those who proceed on the supposition that parasites are harmless ignore the possibility, which always exists, of their not being so, and, in consequence, subject their patients to considerable risk;—which, I venture to say, is incorrect medical practice.

The stock argument against the harmfulness of parasites is that they often occur in apparently healthy persons—an argument of the most unscientific nature. The total sickness produced by parasites must depend on the capacity for mischief produced by each parasite, the number of parasites, and the strength of the patient (paragraph 29); and it is quite possible that considerable numbers of some parasites may exist in strong, well-nourished hosts without causing mischief, while the same parasites in the same or smaller numbers may kill more weakly patients.

It is obvious that a strong, young, well-fed man will support a much larger number of ankylostomes without inconvenience than a cachectic struggling between life and death can. To argue that, because the first endures them with impunity, therefore every one can do so is quite absurd. We cannot fix with certainty the number of ankylostomes required to produce harmful effects—the number is, in mathematical language, a function of several independent variables.

I believe that most medical men who should happen to find themselves possessed of even a few of these entozoa would not delay in ridding themselves of them. Our duty to our patients, then, demands that we use every precaution to detect and expel them from those who are placed in our care.

The drift of these observations must now be obvious. We possess in the microscope an easy and almost sure means of ascertaining the presence of ankylostomes—a means which must not be neglected in cases where the parasites may by any possibility exist. And this leads me to my first recommendation:— *The dejecta of all patients in localities where ankylostomes are present should be examined for the ova of these worms as a routine duty.*

This recommendation applies to many parts of India, to Europeans as well as natives, to soldiers as well as civilians. Remarks as to its feasibility will be made presently. The use of thymol as a diagnostic measure is, of course, not generally excusable when the microscope can be used.

The question of the spontaneous *extinction of the parasitic invasion* in old cases of paludism is one to which I invite particular attention because of its bearing on treatment by quinine. Empirical practice has already discovered that this drug is not so efficacious in advanced as in early stages of the disease. Its effect appears to be solely or chiefly that of a poison to the parasites; and it is clearly unnecessary to employ it in large doses when there are no longer any parasites remaining to kill.

What my observations on kala-azar tend to show is that this stage may be reached very much earlier than, to judge by the continuance of fever, we may be led to expect. In such cases, however, the fever is the *febris secondaria post malariam.*

I am convinced that a similar early extinction occurs in thousands of cases all over India—that the invasion is often nearly or completely quelled at a time when the appearance of daily fever, sometimes of a rather severe type, would lead us to imagine it to be be very active.

In many of the kala-azar cases in which such fever was occurring, the absence of the parasites was proved most conclusively, not only by a failure to find them in repeated examinations of the finger-blood, but by the fact that

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blood from the spleen contained no pigment. Cases 61 and 62 were typical of this condition; and so was case 75, until the final weak invasion, which occurred just before death, set in.

Now quinine in large doses is invaluable during the parasitic stage; but in such doses it is often distressing to the patient, and may even be hurtful at a time when the patient requires good alimentation to support him through the illness. Why then give it when no longer required?

This leads to my next recommendation:—*Before attempting to treat a chronic case of paludism it is necessary to assure oneself as to how far the parasites are still present.*

Regarding the *incidence of kala-azar on the organs* and the *low fever*, I think that malarial fever in all parts of the tropics frequently shows similar phenomena. We must, therefore, not imagine that a case of chronic paludism always consists of nothing else but an invasion by the parasites of the red corpuscle. There is reason to believe that long after these have vanished, the secondary effects which they leave behind them may still destroy the patient. Practically speaking—that is, speaking from the point of view of treatment—most of the cases of kala-azar at Nowgong were no longer cases of malarial fever; they were cases of enlargement of the liver and spleen with a concomitant low fever, and required treatment as such. The treatment which, I think, would commend itself to most practitioners would be that by alkaline laxatives, weak quinine and arsenic, and, above all, the best possible dieting.

I recommend, therefore, that *in the older cases of malarial fever the closest possible attention be paid to the secondary effects of the parasitic invasion.*

These recommendations may, I think, be accepted as being founded on assured facts; my next one, however depends more on hypothesis, namely the hypothesis of *continued pervasion* of the blood by the parasites, advanced in paragraph 29.

Usually, except in such patients as we can keep continually under treatment, quinine is given or taken only during the periods of fever. The patient then doses himself freely; the parasites are destroyed to a certain extent; partial recovery ensues, and the drug is no longer employed. But presently, no longer being checked by the quinine the parasites multiply again and another attack of fever ensues—to be treated in a similar manner. Such treatment appears to me to be quite insufficient; correct treatment would aim not at reducing the parasites temporarily, but at exterminating them altogether.

The question whether the parasites during the apyrexial periods undergo encapsulation or continue to propagate themselves as usual in small numbers, is important as regards treatment, because in the former case quinine may be useless during such periods, and in the latter case small doses, persisted in for a long time, should suffice to conclude the infection. I believe in the latter alternative for many reasons; and therefore recommend as follows:—*Quinine should be given continuously for weeks or even months after an attack of (parasitic) fever.* Small doses (up to 10 grains daily, according to the patient's amenability to the drug) generally suffice, if given with great regularity; especially if given in the morning, just before breakfast. I can speak with experience of this method, which I have frequently used. On the other hand, I generally find that it is those patients who take quinine only when they "are getting fever" who suffer most from secondary effects.

The examination of the blood for the parasites of malaria, though quite easy to those who have mastered the *technique*, is not so easy or rapid a process as the examination of dejecta for the ova of intestinal parasites. Moreover, while always useful, it is not absolutely necessary when the typical fever suffices to establish the nature of the disease. Hence I hesitate to recommend its adoption as a routine. But in doubtful cases, and in old cases of paludism, where it is necessary for the purpose of treatment to ascertain how far the symptoms are secondary and how far they are still being caused by the presence of parasites, correct practice demands a search being made for the organisms. Further than this, in some doubtful cases where no parasites can be detected in the peripheral blood, or where there are severe secondary symptoms which may be due partly to a small remnant of the parasitic invasion, exploration of the spleen for parasites or recent melanin is advisable. Hence I recommend

that *search for the parasites of malaria or for melanin should be carried out where required for purposes of treatment.*

These recommendations for diagnosis and management in paludism may be collected in a more orderly manner, as follows :—

1. Search for the parasites of malaria or for melanin should be made when required.

2. Early cases, in which the parasites are found by the microscope or are inferred to exist from the presence of the typical fever, must be treated by large doses of quinine (given if possible an hour or so before the birth of each fresh generation of the organisms).

3. Quinine in smaller doses should be rigorously continued after the febrile period, long enough to ensure the final extermination of the parasites from the system.

4. In older cases, it is necessary to ascertain how far the parasites are still present. If found, they must be exterminated as soon as possible by large doses of quinine. If not found, we have still no right to infer that they are absent; and should, therefore, exhibit small doses of quinine daily for weeks or months on the chance that some of them still remain.

5. Crescents do not produce fever; continued small doses of quinine are required when they only are present.

6. In other cases, we must always remember the possibility of any fever which may exist being wholly or partly a *secondary fever*, especially if it exhibit the characteristics given in paragraph 32, and if the spleen or liver are enlarged. It should be treated by daily small doses of quinine to ensure destruction of any parasites which may still be present, and by attention to the state of the organs to which this kind of fever appears to be due.

7. If the spleen be much enlarged, there is a presumption, as regards natives of India, that the parasitic invasion is quite or nearly exhausted; and this presumption is strengthened if there be no more attacks of the typical malarial fever. In such cases attention should be devoted particularly to the state of the organs; large doses of quinine will probably be found useless if not harmful; and we should depend on laxatives, tonics and good food—especially, I think, fresh milk.

8. In the last stage, dieting and attention to the frequent intercurrent complaints, such as diarrhœa, dysentery and worms, must be depended on.

9. In all cases of chronic malarial fever, microscopic examination of the dejecta for the eggs of worms, especially of ankylostomes, is an absolute necessity. And the examination should be repeated a week and more after vermifuges have been given, in order to ascertain whether any worms remain. The employment of thymol in large doses without previous examination of the dejecta is not as a rule defensible, unless the latter course cannot be adopted.

It will be perceived by the experienced practitioner that many of these counsels are "counsels of perfection," which can more easily be written down than followed; nevertheless, an attempt can be made to follow them in a large number of cases.

I have recommended the microscopical examination of the dejecta as a routine, and of the blood when necessity arises. It may be objected that these recommendations are impracticable and that medical men have no time to carry them out.

The examination of the dejecta is an extremely easy process, requiring only the humblest instruments and capable of being performed by all hospital assistants. Any medical officer can easily train his subordinates in a few days to do the work; and after that only his superintendence will be required. The *technique* is merely to place a small portion of the dejecta with a piece of stick in a drop of water on a glass slide, to impose a cover glass, and to examine with a medium power. The eggs of the different worms are figured in the text-books [14 and 26]. In my experience, medical subordinates soon take considerable interest in the task; and, in short, there is little excuse for not making these very necessary examinations.

The examination of the blood, however, requires high powers of the microscope and some experience. Medical subordinates can do this work also, as I have found; but the medical officer must first be himself well acquainted with the subject. Though I certainly do not think it necessary, or even possible

to examine the blood of every simple fever case which comes to hospital, I do think it necessary for all medical men practising in the tropics to make themselves familiar with this, the most important part of the study of the most important tropical disease. It is impossible to ignore the exigency of this duty, however troublesome it may be.

I should like to commend to those who care to undertake research the further study of the secondary fever; and to those who have opportunity for making autopsies, the condition of non-pigmented enlargement of the spleen.

42. Official Recommendations.—With regard to the prevention of the present epidemic of kala-azar, I have little to add to the recommendations of Captain Rogers in Section X of his Report, which I beg to endorse.

I am of opinion that kala-azar is communicable from the sick to the healthy in some indirect manner, and that the infection tends to cling to houses.

I think also that there is a certain external condition required for the extension of the disease—probably the presence of some particular species of mosquito or other suctorial insect.

Any attempt to control the epidemic by the elimination of this external condition is not likely, in the present state of our knowledge, to be successful.

It is necessary, then, as regards preventive measures, to treat the disease simply as a communicable one, and as one the infection of which adheres to dwellings—in other words, as a disease which spreads in a manner somewhat similar to plague.

The measures already proposed by Rogers appear to me the only ones likely to affect this; namely, (1) the control of communication between affected and healthy sites; and (2) the vacation of infected sites.

I have been informed by Drs. Lavertine and Price that these measures appear to have been successful to a large extent in the tea-estates near Nowgong.

In my opinion, however, based on a considerable experience, no measures aimed at controlling epidemics in India are likely to be successful unless placed in the hands of capable officers specially deputed for the purpose—as in the case of plague.

One or more energetic medical officers employed in this manner may be able to do much. If it be found feasible to make such appointments, the organisation may be briefly as follows:—

(1) Each special officer should be placed in charge of a locality where numerous cases of early kala-azar or severe fever are occurring.

(2) Hospital assistants who have now been allotted to village dispensaries in that locality should be placed under his orders.

(3) It should be his duty to make himself acquainted with the incidence of the disease in his district; to conduct any preventive operations which may be decided upon; and, above all, to superintend closely measures of medical relief in the most acutely-affected villages.

Frankly speaking, I do not think that any organisation falling short of this is likely to be of much avail. If one junior medical officer be appointed for a preliminary trial, the cost will not be much, as numerous additional subordinates are already employed on the duty.

I lay particular stress on medical treatment, because I believe that much can be done in this line if, and only if, the treatment be carried on under close European supervision. I refer specially to the treatment of early cases of fever by quinine. If camp dispensaries, under hospital assistants and supervised by the special medical officer, be placed near to villages where acute fever is raging; if the special officer be sufficiently active to visit these dispensaries frequently in turn and to attend personally as often as he can to the fever cases; if the patients be encouraged by his influence to take quinine freely, I think it likely that a great saving of life will result. I say early cases of fever, because the old cases of cachexia are probably beyond treatment by quinine; hence the most recently affected villages should be selected for the experiment.

It would be fatal to the experiment to give the special officer too large an area to work over. An extension of the method could be adopted if the first results be at all encouraging.

The special officer should be allowed to move his own subordinates according to his discretion. His time should on no account be taken up by the compilation of returns. He should be encouraged to make all suggestions which he thinks fit to offer. He should understand that his duties extend to the care of patients and the prevention of the disease where practicable; and not to scientific research, except in the second place. He should know how to use the microscope for the treatment of malaria and ankylostomiasis. He and his subordinates would probably require tent equipage.

A call for volunteers for the duty would probably permit of a good selection being made.

I do not know whether this scheme will be considered feasible. I fear, however, that I can suggest no other which is at all likely to have any influence in checking the present epidemic of kala-azar.

But as I have frequently pointed out, the questions with which we are concerned in kala-azar apply also to malarial fever in general; and as my present duty extends to a consideration of this, I think I should take the present opportunity to draw attention officially to a very important matter—referred to in the preceding paragraph—the proper scientific method of diagnosis in malarial fever and ankylostomiasis.

In the use of the microscope science has given us a means of diagnosis in these diseases which generally far exceeds in accuracy the old symptomatological methods, and which is frequently essential to the correct treatment of patients.

In the opinion of every authority on these diseases these means should be often employed; that is, I think, as a routine as regards ankylostomiasis, and, when necessary, as regards malarial fever.

The intestinal worm called ankylostomum duodenale, which lives by suction of the blood, is known to be widely prevalent in India, and causes, directly or indirectly, a mortality the extent of which will only be gauged when the microscope is generally used for its detection; while malarial fever is well known to be the most important of tropical diseases.

Many medical men now employ the microscope in the diagnosis and treatment of these diseases; and the time appears to be ripe for urging its general use by the profession. I beg, therefore, to recommend that the medical services in this country be encouraged gradually to introduce the method referred to into ordinary practice.

For this, the following measures may be suggested:—

(1) All medical officers may be urged to make themselves gradually familiar with the necessary *technique* — a matter of no great difficulty, since a large number are already acquainted with it.

(2) Thorough *practical* instruction in this matter should be given in the medical schools in this country. Medical subordinates already in the employment of Government should be instructed as opportunity offers by the medical officers under whom they are serving.

(3) In localities where ankylostomes are prevalent, small, strongly-made microscopes of weak powers, suitable for the detection of the eggs of these and other intestinal worms, should be issued to all dispensaries. Such microscopes may, I think, be manufactured in Europe for the purpose, at the cost of about ten to twenty shillings each—possibly at a lower cost if ordered in large numbers.

(4) More powerful microscopes, provided with lenses suitable for the examination of blood, should be possessed either by all commissioned medical officers or by all hospitals, Civil and Military, where such medical officers are employed.

With reference to (2), I think it advisable to mention that during the course of my present studies I have come cross two medical subordinates in charge of dispensaries who, though many of their patients were then suffering from the worst degree of ankylostomiasis, informed me that they had never even heard of the disease. They certainly know nothing about it; were not acquainted with the microscopical method of detecting the worms; had no microscopes to use for the purpose; and were, in fact, treating these severe cases of the disease with tonics for "malarial cachexia." Similarly, I have generally found medical subordinates in this country to be quite insufficiently instructed in regard to tropical parasitology — that is, in regard to what are

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perhaps the most important diseases in the country. I venture to recommend that instruction in these matters should not only be theoretical, but should extend to the practical detection of the parasites by the microscope; and can vouch for it from personal knowledge that native subordinates are quite capable of doing the work if taught how to do it.

A more general use of the microscope, especially for the detection of intestinal parasites, is, I am confident, very urgently demanded in tropical medicine.

I have not made these last recommendations lightly; carrying them out will involve some expense to Government and some trouble to medical officers; but it is difficult to escape from the fact that until they are carried out patients will have just cause to complain that they are not being treated by the best methods.

Conclusion.

The great length of this report is due to the necessity which has arisen for investigating and discussing the amphibolic *febris secondaria*, and the condition of unpigmented enlargement of the organs found in kala-azar. I trust, however, that the attention here drawn to these apparent anomalies will be of some general use in tropical medicine.

Owing partly to the labour involved in this work and partly to the plague scare in Bengal having greatly enhanced the difficulties of carrying out experiments with human malaria, I have failed in repeating my original cultivations of the human parasites in mosquitoes, although many attempts with dappled-winged and other insects have been made. Fortunately, however, I am able to conclude this report with the statement that Grassi, Bignami, and Bastianelli have been more lucky in Italy. Some of my preparations of proteosoma in the mosquito, together with copies of my reports on the subject, were sent to these observers last autumn; and they at once essayed the cultivation of the human parasites according to the methods enjoined by Dr. Manson and employed by me. They were immediately successful; and found that both the æstivo-autumnal and mild tertian parasites are cultivable in an Italian species of dappled-winged mosquito, the *Anopheles claviger* or *maculipennis*. Their results are published in a paper [41], dated the 22nd December 1898. As anticipated by me, the former parasite produces germinal threads which, like those of proteosoma, enter the veneno-salivary gland of the insect. Hence the last possible doubt as to the communicability of human malaria has been removed.

Black spores have also been observed in the mosquito stage of the human parasites; but some recent observations of mine tend toward throwing doubt on the exact nature of these bodies.

My thanks are due to Captain McNaught, Dr. Lavertine, Dr. Dodds Price, and Major Macnamara for their valuable statements; and also to Dr. Daniels for his assistance in regard to the sections, and especially for his having been so kind as to place at my disposal the results of his numerous autopsies—results which have so important a bearing on the difficulties met with in kala-azar.

I must also express my indebtedness to Colonel Calthrop, Principal Medical Officer, Assam, for the services of a medical subordinate; and to W. J. Reid, Esq., I.C.S., lately Deputy Commissioner, Nowgong, for assistance rendered in many ways.

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On Special Duty.

Calcutta;
The 30th January 1899.

REFERENCES.

B. M. J. = British Medical Journal.
I. M. G. = Indian Medical Gazette.

1. Ross, Cultivation of Proteosma in Mosquitoes, I. M. G., November and December 1898.
2. Ross, Infection of Birds with Proteosoma, I. M. G., January 1899.
3. Giles, Report on Kala-azar, Assam Secretariat Press, 1890.
4. Rogers, Report on Kala-azar, Assam Secretariat Printing Office, 1897.
5. Rogers, The Burdwan Epidemic Fever, I. M. G., November 1897.
6. Review and Editorial on Rogers' Report, I. M. G., December 1897.
7. Giles, The Etiology of Kala-azar, I. M. G., January 1898.
8. Editorial on Kala-azar, I. M. G., January 1898.
9. Thornhill, Criticism of Rogers' Report, I. M. G., February and March 1898.
10. Giles, Kala-azar, B. M. J., 26th March 1898.
11. Royal Medical and Chirurgical Society, Discussion on Kala-azar, B. M. J., 26th March 1898.
12. Rogers, Reply to Criticisms, I. M. G., June and July 1898.
13. Giles and Thornhill, Alleged Infectiousness of Malaria, I. M. G., January 1899.
14. Manson, Tropical Diseases, 1898.
15. Dobson, Prevalence of the Dochminus Duodenalis, I. M. G., December 1892, and January and February 1893.
16. Harold Brown, Kala-dukh, I. M. G., September 1898.
17. Williams, Prevalence of the Ankylostoma in Madras, I. M. G., May 1895.
18. Ross, Malaria, Amœba Coli and Cercomonas, I. M. G., May 1897.
19. Powell, Prevalence of Certain Intestinal Parasites in India, I. M. G., December 1898.
20. Thornhill, Ankylostoma Duodenale, I. M. G., September 1895, *et seq.*
21. MacCallum, Changes in Organs of Birds infected with Hæmatozoa, Journal of Experimental Medicine, Vol. III, No. I, 1898.
22. Marchoux, Le Paludism de Sénégal, Ann. Inst. Pasteur, 1897.
23. Ross, Malaria Parasites in Secunderabad, B. M. J., 1st February 1896.
24. Marchiafava and Bignami, Summer-Autumn Malarial Fevers, New Sydenham Society, Vol. CL., 1894.
25. Laveran, Traité du Paludism, 1898.
26. Davidson, Hygiene and Diseases of Warm Climates, 1893.
27. Thayer, Lectures on the Malarial Fevers, 1898.
28. Mannaberg, the Malarial Parasites, New Sydenham Society, Vol. CL., 1894.
29. Vandyke Carter, Blood-Orgainsms in Ague, Scientific Memoirs by Medical Officers in India, 1887.
30. Crombie, Address at Indian Medical Congress, I. M. G., January 1895.
31. Crombie, Treatment of Malarial Fever, I. M. G., February 1896.
32. Maynard, Examination of Malarial Blood, I. M. G., November 1895.
33. Rogers, Etiology of Malarial Fever, I. M. G., February 1896.
34. Murray, The Malarial Parasite at Lahore, Scientific Memoirs of Medical Officers in India, 1897.
35. Sturmer, Types of Malarial Fevers in Madras, Transactions of South India Branch of the British Medical Association, July 1897.
36. Kelsch and Kiener, Traité des Maladies des Pays Chauds, 1889.
37. Daniels, Papers on Ankylostomiasis and on Pigmentation of the Organs, the British Guiana Medical Annual, 1895.
38. Landois and Stirling, Text-book of Human Physiology, 1891.
39. MacCallum, Hæmatozoan Infections of Birds, Journal of Experimental Medicine, Vol. III, No. 1, 1898.
40. Grassi, Bignami and Bastianelli, Coltivazione delle Semilune Malariche dell'uomo nell Anopheles claviger, Fabr., Reale Accad. dei Lincei, Roma, 28th November 1898.
41. *Ibid*, Further Researches, *ibid*, 22nd December 1898.

APPENDIX A.—STATEMENTS.

1. Statement of **Sri Jut Gunahash Gassawmi**, Tahsildar of Roha; formerly suffered from kala-azar; now recovered; case (66). Taken on the 23rd September 1898.

"I was living at Naukla when I was taken ill; my family lives at Nowgong. I was the first in my family to suffer—in October 1892. Disease began with a feeling of uneasiness for three or four days; then a sudden attack of severe shivering commenced, gradually followed by severe fever on the same day. Could not perspire for two days. Had a remission on the third day, when I perspired on the forehead only. Was better for two or three days, but am certain that the fever was continuing the whole time. After that the fever came every day, often preceded by shivering, not so severe as at first. After a fortnight, left Naukla and came to Nowgong (a distance of 38 miles). Came under Dr. McNaught's treatment. Was four months in Nowgong, during which the fever continued off and on and much reduced me. The spleen and liver were both found to be enlarged by Dr. McNaught on my arrival at Nowgong, and afterwards enlarged much more. After three or four months my legs began to swell. On the fifth month went to Benares and Delhi. After leaving Nowgong felt better gradually. Then the fever disappeared, liver and spleen diminished, and I slowly became quite well after continual change of scene. My health is now better; and I am fatter than I was before the illness. Since then I have several times had ordinary fevers. Had no diarrhœa or dysentery when I was ill. During my illness the fever used to be sometimes severe and sometimes light. I think I should have died if I had not left Nowgong.

My family consisted of 19 people, of whom eight got the disease and 11 did not. My sister, nephew, niece and one cousin all died; one nephew, two cousins and my father's sister all had it and recovered. They suffered from kala-azar. My sister was attacked during my illness, when I was at Nowgong (in the same house with her—R. R.), and died in seven months. My nephew was next attacked, a few days before I left the place; and died. The others were attacked after I left Nowgong for Benares. All the members of my family referred to above lived in the same premises. Besides them, seven servants died of kala-azar, three recovered, and 11 were not attacked. From what I saw and have heard about all these cases, so far as I can remember, all had fever with shivering, and enlargement of the spleen, etc. I do not remember that any of the cases consisted merely of weakness without any fever. I am sure that my sister and nephew had fever. Relations living close by were also taken ill (? first)."

Note.—The patient was attacked at Naukla and brought home to Nowgong by his parents, where his sister and others were next attacked in succession.

2. Statement of **Captain McNaught**, Civil Surgeon of Nowgong. Taken on the 18th October 1898.

"I was appointed Civil Medical Officer to the Garo Hills, Assam, on the 5th February 1880. I find there is no mention of kala-azar earlier than in the Provincial Report for 1881; in which year, in a note regarding Tura, Garo Hills, p. 38, kala-azar is first mentioned. I was directed to make a special tour of enquiry into the country affected in 1882, and my report was embodied in the District Sanitary Report of Assam for 1882. I then described 120 cases of the disease and the conditions in which it appeared. I continued to see the disease in the Garo Hills up to February 1885, practically five years. Then I came to Nowgong. The disease was not heard or known of in district villages or tea-gardens here at that time. It did not appear in the district until 1889. It slowly increased, and then began to rapidly extend itself all over the district, showing itself first at isolated points, which became more numerous and finally coalesced, until the whole district was affected. At the beginning of the epidemic in 1889, the people themselves on two occasions sent petitions to the Deputy Commissioner asking that measures be adopted to prevent affected persons being allowed into the district. I have seen very numerous cases ever since, both at the dispensaries as in and out-patients and at their homes in the villages.

"From my own observations and frequent enquiries both from the affected persons and their relatives, I am perfectly convinced that the disease popularly known as kala-azar both in the Garo Hills and here was the same disease; that it begins with fever, often severe, sometimes very severe, sometimes commencing with rigors, sometimes with mere chilliness; the fever being sometimes continued, more often remittent, not, as far as I know, intermittent. The fever lasts for 10, 14 or even 20 days, during which period the spleen and liver become slightly enlarged and often painful, sometimes probably even in a condition of inflammation. There is then generally an apyrexial period which lasts for a week or two or more, indefinitely, during which period the spleen and liver still remain enlarged and give trouble to the patient. So far as I have been able to observe, no treatment by antiperiodics, quinine, salycine, methylene blue, arsenic, picrate of ammonia, has been able to prevent a second attack of fever. The second attack comes on, in my experience, with certainty, but does not, so far as I know, begin with rigors, though aching of the limbs, and so on, is usually present. During this period the spleen and liver both continue to enlarge, and are often painful, not only on

palpation—the patient himself complaining of pain in them. This attack of fever remains indefinitely for various periods. In many cases there is then another apyrexial period, followed again by a similar attack. This history is repeated on several occasions. The spleen and liver have now become much enlarged and easily visible through the emaciated parietes of the abdomen. At the same time, with the first and second attacks, anæmia may be present in some instances, but is never very marked. As the attacks recur, anæmia may become more marked; but in most cases never reaches any high degree, the tongue generally remaining red. Anæmia is by no means a leading characteristic of the disease. By this time emaciation has become marked, while the superficial veins of the epigastric region are enlarged. The patient now suffers from a low form of fever which remains for weeks and even months. In many cases there is epistaxis, which is sometimes controlled only with difficulty. This condition remains for months. Dropsy of the face and in some cases moderate ascites are present; in rare instances there is puffiness of the eyelids and face. There is undoubted darkening of the skin in many cases from my own observation; and this is also stated to be the case by the relatives. According to my observations, this symptom is visible only in the more advanced cases. Jaundice may occur with the earlier attacks, but is not common. At any time during the illness, but more especially after two or three attacks of fever, there may be intercurrent affections, such as bronchitis, pneumonia, diarrhœa and dysentery; but these do not always occur. Sometimes, during the chronic stage, there is a sudden attack of high fever, not necessarily, I think, due to pneumonia, which not infrequently terminates the case.

"Further on, in the chronic stage, the low fever disappears, and often there is a decrease in the size of the organs; but the emaciation and darkening of the skin remain. The patient is able to go about, and complains of nothing but debility and perverted appetite; especially a desire for animal food, which is so marked that good class Hindus will take forbidden flesh. The emaciation progresses until the man is sometimes a walking skeleton, the temperature often being subnormal. If an attack of diarrhœa or dysentery does not terminate the case, the patient generally dies of asthenia.

"I think that death may occur even during the first attack of fever or at any later stage, but oftener after several attacks, and still more frequently in the advanced stages. The general duration of the disease is from six to nine months; though I have known cases to last years.

"Recovery may take place at any stage except perhaps the last ones; but very few recoveries occur."

In answer to questions:—

"I think that enlargement of the liver is present in every case. It is a marked feature of the disease. The spleen is enlarged in every case; sometimes it is simply enormous. I have never seen suppuration in these organs in cases of kala-azar. If recovery ensues, the enlargement of the spleen and liver may disappear entirely. I have never known "black-water" occur in kala-azar, but I have known three cases amongst Europeans in the tea-estates. I know several cases of kala-azar which have been treated with quinine from the earliest stages and which have not recovered. A dozen cases at least in this district alone. The doses were 10, 12, 16 grains daily, generally in the morning. Some of the cases took over an ounce of quinine altogether and died finally. The popular belief is generally that quinine is not only useless but harmful."

Q. How soon after the actual beginning of the case, do you remember, was this treatment commenced?

A. Within a few days; after the usual preparatory treatment by purgatives, ipecacuanha and antipyretics.

Q. Is there any change in the local conditions which may account for the epidemic? Do Europeans suffer as much as natives?

A. No change whatever. Europeans suffer less frequently; but I have seen some attacked.

Q. Before kala-azar commenced here, were chronic malaria and malarial cachexia not to be seen?

A. There were cases — but few. When I came here it did not strike me that the population was by any means a malaria-stricken one.

Q. How do you distinguish between kala-azar and malarial fever in their earlier stages.

A. It is most difficult to make this distinction during the first attack. But when a second and other attacks occur with marked enlargement of the spleen, and especially of the liver also, in a family in a locality known to be affected with the disease, the presumption that it is kala-azar gains ground, especially when anti-malarial treatment fails to prevent the recurrence of fever.

Q. How do you distinguish between kala-azar and malaria in their more chronic stages?

A. It is most difficult to do so, apart from the history of the case showing that it occurred in a kala-azar-stricken house or locality.

Q. Generally speaking, what differences are there between kala-azar and malarial fever?

A. (1) Kala-azar is more fatal. (2) It is more intractable to treatment and is not cured by quinine. (3) It is certainly communicable from the sick to the healthy; it runs in families and is epidemic — which, so far as I know, cannot be said of malarial fevers.

Q. Do you think kala-azar is ankylostomiasis?

A. No, absolutely and entirely different.

Q. Are you quite certain of the identity of kala-azar as described above?

A. I am quite certain of it — from my own experiences in the Garo Hills and in this district, and from reports of others in other districts. The people themselves are perfectly familiar with the disease. I am quite sure that it is primarily a fever with enlargement of the spleen and liver; and the people themselves give exactly the same account.

Q. Do you know Assamese well?

A. Yes; I have passed the lower and higher standards.

Q. Do you know Garo?

A. I have passed the examination in that also.

Q. Have you any remarks to add?

A. Along with the symptoms of kala-azar described above, a few of the cases present symptoms of excessive anæmia and marked dropsy, which, in my opinion, are due to the combination of ankylostomiasis with kala-azar. These symptoms are, I find, in proportion to the number of worms and to the length of time the patient has been suffering from them. In autopsies of kala-azar I generally find a few ankylostomes (20 or 30), but rarely as many as three or four hundred. In some cases they are quite absent. I have sometimes found the worms in small numbers in healthy medico-legal cases. Anæmia with dropsy had been very prevalent formerly in tea-estates, though it has not been recognised as ankylostomiasis until comparatively lately. I am sure that owing to this recognition and the appropriate treatment there is now a most marked diminution of these cases.

Menstruation is checked in the advanced cases of kala-azar. It is the popular belief that males are more affected than females, and that there are more widows than widowers in the villages.

Before the appearance of the epidemic, ankylostomiasis was very prevalent in the tea-estates. It was not prevalent in the villages.

3. **Statement of Dr. J. C. Lavertine.**—Taken in the presence of Dr. Price on the 23rd October 1898:—

"I have been seeing kala-azar since March 1894 in the Nowgong District. I am absolutely certain about the identity of the disease. I am certain that it is a disease which is communicable from the sick to the healthy. The communicability varies directly as the degree of proximity; and the infection clings about houses.

"The disease begins always with fever, which may be remittent or intermittent, and is rarely preceded by rigors; but mere chills occur sometimes, especially in the intermittent forms. The fever is generally severe at first; it may vary between the limits of 95°F and 106°F.

"It may last from three weeks to three months. There is then an apyrexial period; followed by another go of fever which may last a variable period. There may be a second and third similar attack.

"Both spleen and liver begin to enlarge generally three or four weeks after the beginning of the illness, and are tender on pressure. The tumefaction of the spleen generally reaches a large size, sometimes an extreme one. The liver also is invariably enlarged, and I think that most frequently the enlargement is on the upper surface. When the enlargement of the the organs has reached a certain degree, I observe that the temperature, as a rule, remains above normal night and day.

"At this stage icterus may or may not (as a rule, not) be present. Epistaxis is fairly common. Dropsy of the feet, ascites, puffiness of the face, are rare at this stage. Emaciation commences at the first stage and progresses continuously, becoming finally very marked. Anæmia at first is not very marked; but it becomes so as the illness progresses. There is an access of anæmia with each attack of fever, with improvement in the intervals. I think that blackening of the skin commences from the very first. I have personally known cases in which it has quite undoubtedly occurred. It cannot be explained by mere dirt of the skin. The lustre of the skin is gradually lost, and the epidermis acquires the appearance of a grate which has been black-leaded but not polished.

"There may be a third stage during which the enlargement of the spleen and liver continue, but in which the temperature becomes subnormal. The tendency to symptoms of diarrhœa and dysentery, always existent from the beginning of the disease, is greater at this stage. There is now extreme weakness and emaciation; also extreme anæmia, more so, I should say, even than in ankylostomiasis; though the tongue may remain fairly red to the end. I no not think the kala-azar cases develop pneumonia; but that the converse sometimes occurs.

"Death may happen at any stage. During the earlier stages it may occur with great suddenness—either from diarrhœa, or some unascertained cause, or from severe fever. In the third stage, death is asthenic, and due generally to very malignant cancrum oris which originates during the period when the temperature is subnormal and the tumefaction of the spleen and liver continues."

Q. How do you distinguish between kala-azar and malarial fever in their earlier stages?

A. I think it is impossible.

Q. And in the later stages?

A. By the extreme degree of enlargement of the organs and of the anæmia, emaciation and darkening of the skin; and, I think, by the comparative absence of œdema. Also by the fatality, the resistance to quinine, the frequency of cancrum oris, and the communicability of the disease.

Appendix A

Q. What effect does quinine have ?

A. Not the same as in malaria, even given up to 30 grains three times a day, and even if given at the outset of disease, that is, after four or five days.

Q. Have you seen " black-water " in kala-azar ?

A. Never.

Q. Do you think that kala-azar is ankylostomiasis ?

A. No, certainly not. They are quite different diseases ; though a kala-azar patient may have any number of anklostomes.

4. Statement of **Dr. D. F. Dodds Price** in additon to that of Dr. Lavertine, taken on the 23rd October 1898.

I have seen kala-azar (in this district) only since January 1893. My experiences agree with those of Dr Lavertine, except in a few particulars which are as follows :—

" (1) As to the communicability, I do not think for an instant that the disease is communicated directly from patient to patient, but from the patient to a second agency, such as the ground, house, bedding, and the like ; and from this agent to a healthy person. The burning roof of a house has been dropped into it and the floor dug up, the walls and the ground outside remaining untouched, without the infectiousness of the premises being destroyed.

" (2) I do not at all agree that the anæmia, even in the worst cases of kala-azar, is so severe as in ankylostomiasis. I have never seen the hæmoglobin below 30° by Gower's apparatus ; while that of parallel cases of ankylostomiasis is often at 20° and has been known by me as low as 12°. The average for coolies should not be taken higher than 65°.

" (3) With regard to pneumonia, I have known a good many cases get it in the cold weather, not in the rains. I have seen several cases die of hyperpyrexia in Dr. Lavertine's second stage. Bowel troubles generally occur in the later stages of the disease, and have carried off the bulk of my patients. I have lost only a few from cancrum oris.

"(4) I think that kala-azar has become modified during the last years, becoming briefer and more severe, but not so common.

"(5) I thiuk that in kala-azar the liver is much more enlarged than in chronic malaria. "

Q. Is kala-azar ankylostomiasis ?

A. No, certainly not. But mixed cases, of course, occur.

Q. What are the differences between kala-azar and malarial fever ?

A. I have satisfied myself that kala-azar is malarial fever of a very fatal type, with special incidence on the liver. The communicability of the disease is, however, hard to explain ; but I am certaiu that it exists.

Q. Does quinine do any good ?

A. I thiuk that quinine does do good ; it is difficult to say, because when a case is cured, we have our doubts whether it has been kala-azar. I think that small doses frequently repeated, up to 30 grains a day, are more useful in the early stages than larger single doses. The best results have been obtained from intra-muscular injections.

The following questions were asked of Dr. Lavertine and Dr. Dodds Price together.

Q. Do you both think that large doses of arsenic, gradually increased, are useful ?

A. We have given it up to one drachm of the liquor thrice daily without bad symptoms.

Q. Do you think that kala-azar originates in the cold weather ?

A. No ; we both think that it generally begins in the mouth of March or April.

Q. Do you think that segregation is useful ?

A. We both agree that it is very useful ; both as regards the sick and those who have lived with the sick.

5. Statement of **Major Macnamara, I.M.S.**, taken on the 25th October 1898, at Tezpur.

" I have been 18 years in this province ; for 8 years in Sylhet, 2 years in the Sibsagur District, one year at Gauhati and 5 years in Tezpur. I have seen cases of disease called kala-azar for the last six years. I must have seen some thousands of cases. The symptoms are definite enough for me to give a description of them. I have treated cases. I have known at least three Europeans who have died of it ; and have enquired the history of the disease from native patients, and in some cases from their relatives. I think the disease is communicable from the sick to the healthy. At any rate, the cases appear to occur in connection with each other.

" The disease begins with a severe attack of fever, which I think occurs in every case. The fever is usually remittent, but it may be intermitent. Rigors do not often occur, neither is the fever often preceded by mere chills. The fever lasts about a week. The patient then feels better and gets about. After that he has slight attacks of fever which become more and more frequent ; until eventually his temperature never falls to normal, lying between 99° and 101°F., though the patient is generally unconscious of it. Three months after the fever has begun, the spleen always, and the liver in about one-third of the cases, begins to enlarge, and in the majority of the cases may become very big. There is no tenderness in them on pressure and no pain, though, of course, some discomfort. I have seen cases which I have had every reason to suppose were kala-azar, but in which there has been no enlargement of the liver ; and I have found the same thing in autopsies. In this opinion I know I differ from others. I think that the constant fever first referred to is more apparent in long-standing cases in which the tumefaction of the spleen, or of the spleen and liver together, has been established. The spleen and liver reach their maximum enlargement in about a year and a half. I have never

seen death occur in the earlier stages; it generally takes place after a year and a half or two years. It is then generally due to asthenia and anæmia. I have never seen pneumonia in connection with the disease. Diarrhœa is apt to set in towards the end of the case. I have never noticed a decrease in the liver and spleen towards the end of the cases. The fever is less violent towards the termination; but I don't think it ever wholly disappears. Anæmia begins to become marked about the third or fourth month. I think it is a continuously progressive anæmia. It becomes extremely marked. Œdema sets in at a late stage — of the feet and about the face. Ascites occurs, but I don't think is very marked; it is certainly not always present. I think there is always darkening of the skin, though in the case of natives it is hard to tell with certainty. I do not think it is due to actual pigmentation. Emaciation is very marked, especially in the later stages. The final picture presented is that of emaciation; anæmia; sunken eyes and drawn face; protuberant abdomen due to enlarged spleen, and giving the appearance of an ovarian tumour; abdominal veins enlarged; often dropsical feet; and fever, which, however, may disappear toward the end. I have not noticed epistaxis.

"In my experience quinine does no good, even given in doses of 20 grains every morning. I cannot speak certainly of its effect from the commencement of the disease; but in some cases in which it was certainly used from the beginning, it did not check the illness."

Q. Are you quite sure that fever and enlargement of the spleen are constant features of the disease?

A. Yes.

Q. How do you distinguish between kala-azar and malarial fever?

A. By the place where the patient has come from; by the fact that he goes from bad to worse in spite of treatment; and that he eats well. These points may not be distinctive, but my diagnosis is based on a consideration of them.

Q. Judging from the mere picture presented by the two diseases, can you distinguish between them?

A. No, I cannot.

Q. Do you think kala-azar is malarial fever?

A. It is certainly very like it. I have always thought it is malaria; but its mode of spreading is so contrary to one's accepted ideas regarding malaria, that I hesitate to come to any conclusion on the subject.

Q. Do you think the disease is ankylostomiasis?

A. No; it is something quite different; ankylostomes may or may not be present, but they no more cause the disease than do round-worms which also very frequently occur in the cases.

Q. Have you any further remarks to make?

A. It strikes me that the disease is very like what I have read of *surra* in horses. The disease seems to me to spread at the rate of about two miles a year amongst a settled population. I can't say at what time of the year infections most generally take place. I rarely find rigors in Assam fever generally. I give quinine generally in pills or tabloids.

6. Statement of **Dr. C. W. Daniels**, Colonial Medical Service, Malaria Commission, taken on the 18th January 1899, at Calcutta.

Q. Where have you studied malaria?

A. British Guiana.

Q. About how many cases of malarial fever or enlarged spleen have you examined during life for the parasites of malaria?

A. Roughly about a hundred and fifty.

Q. What varieties of parasites did you find in Georgetown?

A. Æstivo-autumnal only.

Q. Did crescents abound in the cases?

A. No; they were rare even in cases kept long under observation and frequently examined.

Q. Do you find parasites as easily in cases of chronic enlarged spleen with pyrexia as in cases where there is no chronic enlargement of the spleen?

A. No; it is very exceptional to find parasites in cases of enlarged spleens with fever or without.

Q. Do you observe in cases of enlarged speen any pyrexia which is not accompanied by the presence of the parasites in the peripheral blood?

A. Frequently.

Q. In cases which have died during or shortly after this kind of fever, have you ever found an absence or only a small amount of melanin in the spleen at the autopsy?

A. Frequently with none; sometimes with little.

Q. What is the nature of the curve of this fever?

A. Very irregular; sometimes transient; sometimes continued; not commonly high; often what would be called a low type of fever.

Q. Is this fever markedly affected by quinine?

A. No; I have given up using it except as a tonic.

Q. Have you observed any tenderness of the spleen during this fever?

A. Often discomfort in the splenic region; but usually not exactly tenderness.

Q. Do you think that the severity of this fever bears any relation to the amount of the splenic enlargement?

A. I have observed no relation.

Q. Do you consider that this fever is due directly to the parasites of malaria?

A. I have no evidence to that effect; rather the contrary.

Q. How many autopsies have you made in tropical countries?

A. About two thousand; in Fiji and British Guiana.

Q. Have you examined the spleen by the microscope for pigment, black or yellow, in many?

A. In about the last sixteen hundred as a routine.

Q. What is the relation found by you in adult Indian coolies between the size of the spleen and the presence of black pigment?

A. A greater proportion of the small spleens than of the large spleens are pigmented; and this difference is more marked with advancing years.

Q. Do you ever find enlarged spleen without melanin?

A. In one series of 207 cases with spleens over 15 ounces, melanin was observed only in 12·5 per cent., while the very large spleens rarely contained it. On the other hand, in spleens of 15 ounces and under, 218 in number, 24·7 per cent. contained melanin.

Q. What of Indian children?

A. The pigmented spleens are generally enlarged.

Q. Did you ever find enlarged spleens without melanin in Indian children?

A. Yes; on several occasions out of about 100 autopsies on East Indians over one month of age and under 20 years.

Q. Have you any evidence to show that melanin never disappears until one or more years after it has ceased to be deposited?

A. No; I have none.

Q. Have you any evidence to show that it ever does disappear before that period?

A. Nothing entirely satisfactory.

Q. Do you think that it ever disappears at all?

A. Yes. In acute infections it is found both in the liver and spleen. In cases where there is no evidence of recent infection, it is commonly present in the spleen and absent from the liver, and *vice versâ* in rarer cases; showing that it may disappear from either organ.

Q. Did you find the liver frequently enlarged in association with enlarged spleen in Indian coolies in British Guiana?

A. Only in acute malaria and pneumonia. In cases of chronic enlargement of the spleen there was usually no enlargement of the liver.

Q. Does the negro race have enlarged spleen as much as the Indian race?

A. No; not nearly so much. But the proportion of spleens which are pigmented is nearly the same, age for age.

Q. Have you been able to study much ankylostomiasis?

A. In Fiji for three years, in British Guiana for six; the disease being very common in both countries.

Q. Do you find enlargement of the liver and spleen in ankylostomiasis?

A. In the liver, the slight enlargement due to fatty degeneration was met with. The average weight of the spleen, however, was rather less than the general *post-mortem* average for the corresponding age. As in other persons, some of the spleens were decidedly above and some decidedly below the average weights.

Q. Do you find any fever in ankylostomiasis?

A. Yes; but many cases are entirely free from it or even have an entirely subnormal temperature. The fever may be of a low continued type; or of a hectic type; or undulatory; rarely going above 102°F—though I have seen it much higher without malarial parasites or black pigment in the organs. The exacerbations are rarely preceded by direct rigors.

Q. Can you exclude malarial fever in such cases?

A. No; because the cases occur in a malarious country. As I have said, the spleen is not enlarged more in a larger proportion of these cases than of the ordinary population.

Q. Do you find yellow pigment and iron in cases of the anæmia of ankylostomiasis?

A. Yes; yellow pigment in the liver invariably; in the kidneys, commonly; very rarely in the spleen. The iron reaction occurs only in about 8 per cent. of the cases; mostly in the liver, but also in the kidneys, and certainly very rarely in the spleen.

Q. Can you exclude previous malaria?

A. No. But such pigmentation was equally common in Fiji, where there were no opportunities for recent malarial infection; and both in Fiji and in British Guiana it was not associated, as a rule, either with enlarged spleen or black pigmentation. The yellow pigment was more abundant in the chronic advanced cases and the iron usually absent.

Q. What other changes do you find in the organs in ankylostomiasis?

A. Fatty degeneration invariably, most marked in the liver, kidneys and cardiac muscles.

Q. Is there emaciation or the reverse in pure ankylostomiasis?

A. Generally no emaciation.

Q. Do you think that the appearance of ankylostomiasis, that is, of the symptoms known to be produced by the worms, is ever determined by an attack of some other disease?

A. Yes; I have known the symptoms to appear suddenly after very mild attacks of dysentery, apparently cured; and have reason for thinking that malaria has a similar effect.

APPENDIX B.

A case, supposed to be kala-azar, reported by Dr. Gibbons. Taken from the *Indian Medical Gazette*, January 1890, page 22.

"Calcutta Medical Society meeting at the Medical College. Dr. J. B. Gibbons showed a liver and spleen which had been removed from a fatal case of Assam fever, probably the kala-azar, which has been for some years attracting attention in the Garo Hills.

"Sainburan, aged about 20 years, a native of Assam, was admitted into the first Physician's ward on the 9th November, and died on the 12th December 1889.

"He stated that he had been suffering from Assam fever for about a year. On admission his condition was as follows:—Very emaciated and weak; complexion sallow; conjunctivæ yellow; liver extended about two and a half inches below the costal arch; spleen enlarged. His temperature on the day of admission was 101·6°F; pulse weak.

"Fever continued until the 28th November, the temperature ranging from normal to 101°F., the evening temperature being generally about 101°F., while in the morning it was lower, and some days normal. From the 25th to 28th he was free from fever.

"On 29th rise of temperature occurred and slight fever was present to the 3rd of December, when the temperature went up to 104°F., and from this date to his death the fever ranged from 100°F. in the morning to 104°F. in the evening, and on one occasion reached 105F°.

"The bowels were constipated during the first fortnight after admission, requiring repeated doses of aperients to produce an evacuation. On the 7th December, mucus and blood appeared in the stools, and from this date he passed several loose bilious stools containing a small quantity of blood.

"He gradually became weaker and died at 9 A.M. on the 12th December 1889.

"*Abstract of post-mortem notes.*—The examination was made six hours after death. Body very emaciated. No subcutaneous fat, no œdema, the peritoneal cavity contained about 16 oz. of serous fluid.

"The liver was large, weight 3 lbs. 3 oz., mottled dark-green and yellow, much congested. Microscopic examination shows great congestion of all the lobular capillaries, but most marked in these belonging to the central veins. The hepatic cells are small, shrunken. granular, and contain minute masses of brown pigment. In some lobules the hepatic cells are completely destroyed, all that remains being an amorphous granular mass. The destruction of the hepatic cells is the most striking feature, the fibrous frame-work is unaltered. The spleen is large, weight one and a half pounds and soft and friable, of a brownish red colour. Sections show extreme congestion but no pigmentation.

"The kidneys are slightly enlarged; the cortex is pale streaked with red; the medulla of a dark-red colour; weight of each four and a half ounces. Microscopical examination; extreme congestion, the renal epithelium is granular and disintegrating; many of the tubules contain masses of broken-down epithelium.

"The mucous membrane of the small intestine was bile-stained in the upper portion; Peyer's patches were healthy.

"The membrane of the whole of the large intestine was thickened and presented innumerable small shallow ulcers, some recent, some of long standing. No worms in the intestines.

"The muscle substance of the heart was pale and flabby.

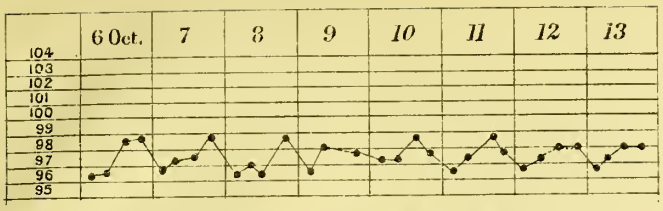
"*Remarks.*—The course and symptoms in this case point to the probability of its being an example of kala-azar. The patient was an Assamese, and only came to Calcutta a short time before he was admitted into hospital. He suffered from enlargement of the liver, spleen and anæmia, recurring attacks of fever and dysentery. These are the prominent symptoms of all cases of kala-azar, vide *Indian Medical Gazette*, January 1889, pages 188-189. Of the *post-mortem* appearances, the absence of pigment in the spleen is noticeable. In all cases of long continued malarial poisoning in Lower Bengal, the spleen contains large quantities of pigment.

"In the liver the destruction of hepatic cells is greater than I have found in any cases of malaria in Bengal."

Note.—In my autopsies, the splenic and hepatic cells were found to be coarsely granular, but no destruction of them was observed by Dr. Daniels or myself.—(R. Ross).

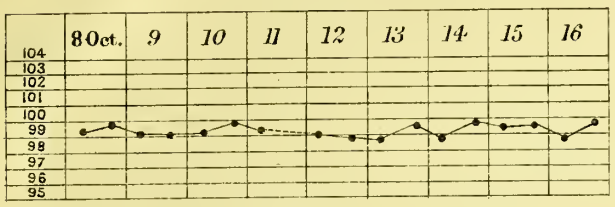
Appendix C. Charts.

Chart 1.



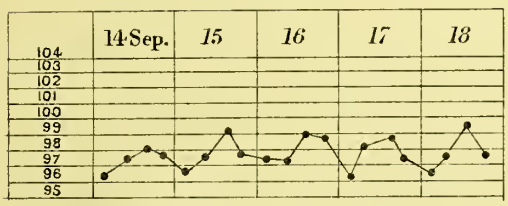
Case 34. Kala-azar. Secondary Fever. Temperatures taken at about 7 a. m., 11 a. m., 3 p. m., 7 p. m.

Chart 2.



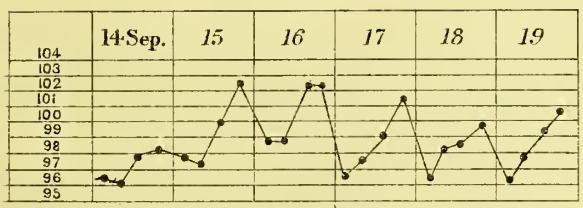
Case 35. Fever. Secondary Fever. Temperatures taken at about 7 a. m. and 4 p. m.

Chart 3.



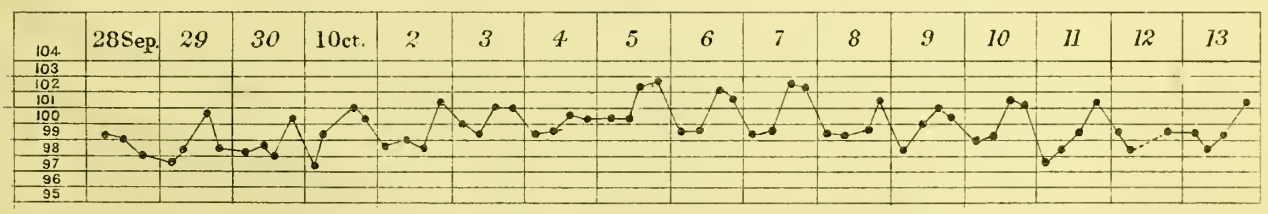
Case 55. Kala-azar. Secondary Fever Temperatures taken as in Chart 1.

Chart 4.



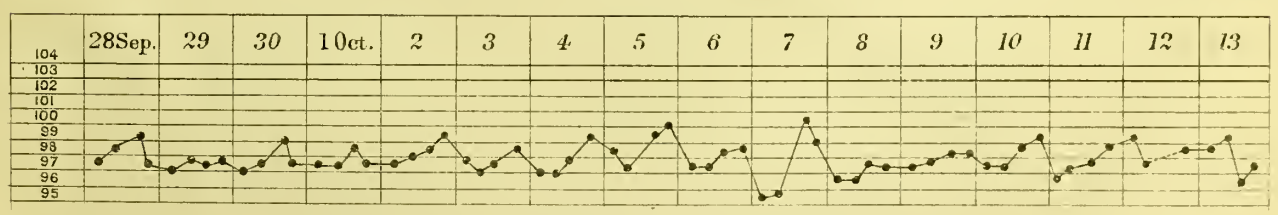
Case 56. Kala-azar. Temperatures taken as in Chart. 1.

Chart 5.



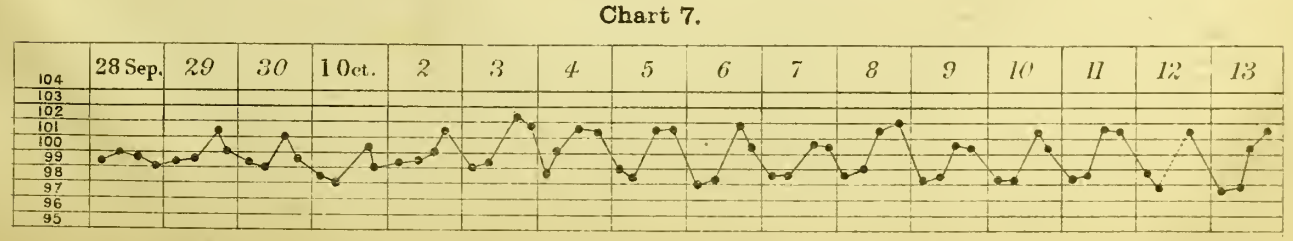
Case 57. Kala-azar. Secondary Fever. Temperatures taken as in Chart 1.

Chart 6.



Case 58. Kala-azar. Secondary Fever. Temperatures taken as in Chart 1.

Chart 7.



Case 59. Kala-azar. Secondary Fever. Temperatures taken as in Chart 1.

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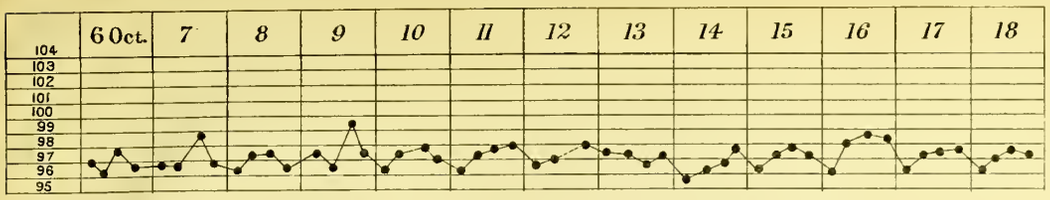
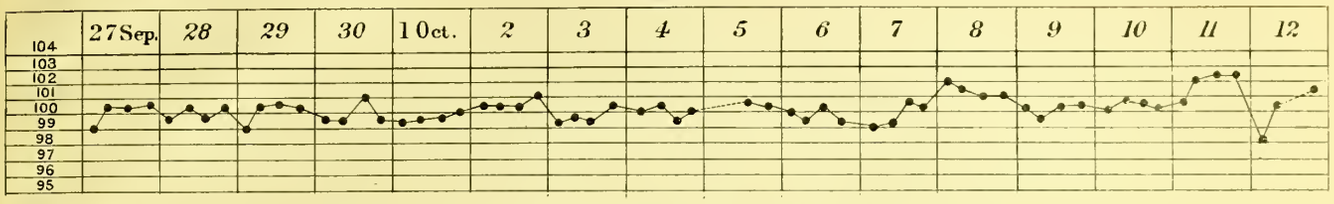
Chart 8.



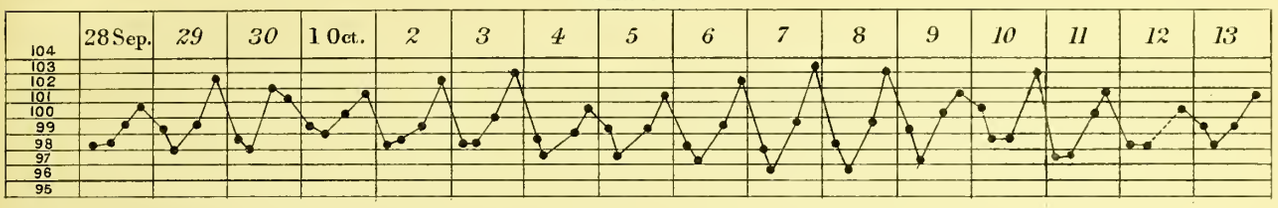
Case 60. Kala-azar. Secondary Fever. Temperatures taken as in Chart 1.

Chart 9.



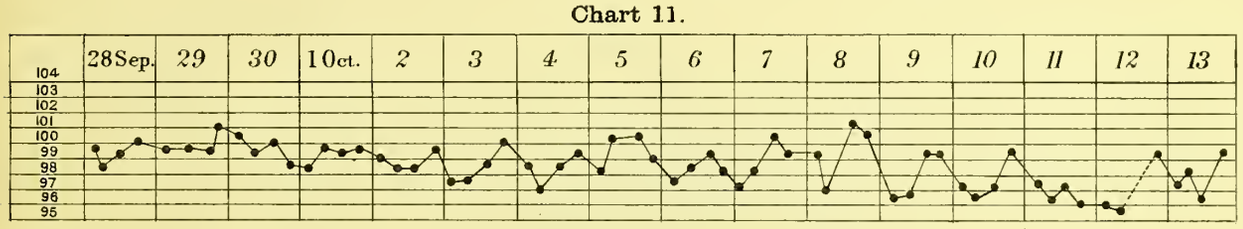
Case 61. Kala-azar. Secondary Fever. Temperatures taken as in Chart 1.

Chart 10.



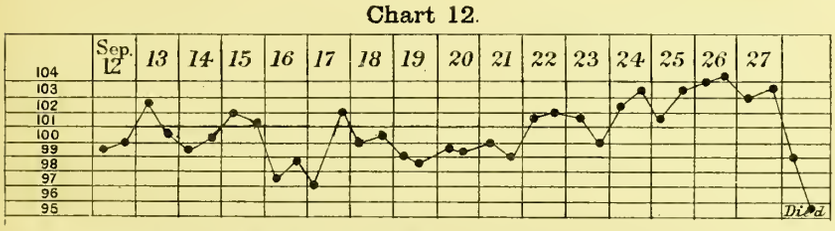
Case 62. Kala-azar. Secondary Fever. Temperatures taken as in Chart 1.

Chart 11.



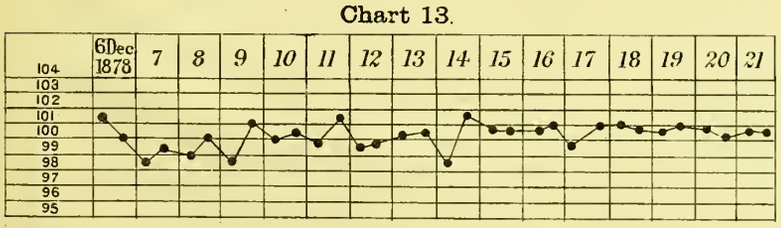
Case 63. Kala-azar. Secondary Fever. Temperatures taken as in Chart 1.

Chart 12.



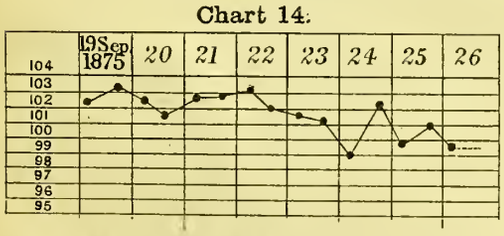
Case 75. Kala-azar. Secondary Fever chiefly, but a very few parasites found on 26th. Organs contained traces of recent pigment only. Temperatures morning and evening.

Chart 13.



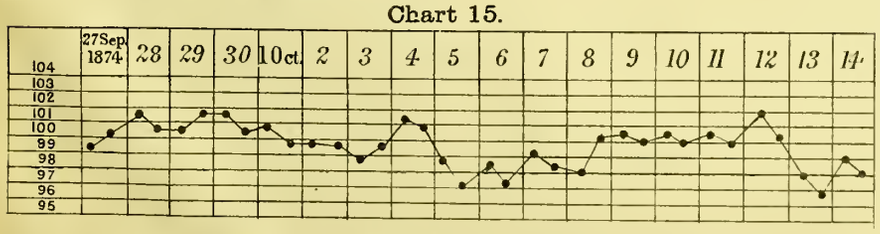
Kelsh and Kiener's Symptomatic Fever [36, p. 566]. Old case of paludism with pain in splenic and hepatic regions.

Chart 14.



Kelsh and Kiener's Symptomatic Fever. Old case of paludism with enlargement of spleen.

Chart 15.



Kelsh and Kiener's Symptomatic Fever. Old case of paludism with great enlargement of spleen and liver.

No. 38, Major Ross.—Feb. 99.—250.

Litho., S. I. O., Calcutta.

REPORT

ON

THE NATURE OF KALA-AZAR

BY

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INDIAN MEDICAL SERVICE.

CALCUTTA:

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